SURGERY
GYNECOLOGY AND OBSTETRICS
An International Magazine, Published Monthly

VOLUME 73 NOVEMBER, 1941 NUMBER 5

SUBCOSTOSTERNAL DIAPHRAGMATIC HERNIAS

Foramen of Morgagni

STUART W. HARRINGTON, M.D., F.A.C.S., Rochester, Minnesota

ONE of the weak regions in the structure of the diaphragmatic muscle as well as one of the weaker attachments of this muscle to the chest wall occurs in the middle leaflet of the diaphragm anteriorly, where, on either side of the sternal attachment in the midline, there are too small apertures caused by deficiencies in the structure of its musculature. These spaces devoid of muscle are triangular with the apex toward the central tendon and the base at the costal margin between the xiphoid process and the pars costalis which starts at the inner surface of the six lower ribs. In some instances the sternal attachment of the diaphragm may be absent or defective, so that the two spaces may fuse into one large opening beneath the sternum and sternocostal junction. These spaces are covered on the thoracic side by pleura and on the abdominal side by the diaphragmatic peritoneum. They are filled with loose areolar tissue and through these spaces pass the superior epigastric artery and lymphatics. These spaces in the anterior portion of the diaphragmatic muscle are called Larrey's spaces and foramen of Morgagni.

From the Division of Surgery, Mayo Clinic.
Read before the Meeting of Western Surgical Association, Topeka, Kansas, December 6 and 7, 1940.

The occurrence of herniations of abdominal viscera through these weak regions into the thoracic cavity has been known for many years. Morgagni is credited with the first description of a diaphragmatic hernia of this type, in 1769, occurring in a patient whom Leprotti had seen in Rome and who died of other causes at an advanced age. At necropsy herniation of the intestine into the thoracic cavity through an opening beneath the sternocostal junction was found, but there was no obstruction of the bowel to suggest that it was a factor in the death, and no signs of injury to the diaphragm were found to indicate a traumatic origin of the hernia.

Hernias of the diaphragm occurring through these regions have received various terminologies such as diaphragmatic hernia through the foramen of Morgagni, or through Larrey's fissure or spaces, and also substernal, retrosternal, parasternal, or anterior diaphragmatic hernia. Inasmuch as these hernias usually occur to either side of the anterior midline of the diaphragm, if an anatomical terminology is to be used, it would be preferable to call them subcostosternal diaphragmatic hernia.

Although the occurrence of this type of diaphragmatic hernia has been known for many years there are relatively few cases reported in the literature as compared with

other types of diaphragmatic hernia. Hedblom (1932) stated that about 60 cases had been reported and Funck-Brentano (1933) stated that 58 cases had been reported in the literature; however, neither author gave bibliographic references of the cases traced or reported. I have reviewed the literature in an attempt to trace the individual case reports and had hoped to have it completed at this time, but there are many duplications of reports and indefinite or inadequate descriptions of cases which have made it impossible to complete the study at this time.

In a review of the literature from 1930 to the present time it was found that 24 cases had been reported, in only 5 of which had operation been performed, in 2 by the abdominal approach, in 2 by the thoracic approach, and in 1 by combined abdominal and thoracic approach. Of the 5 patients on whom operation was performed, 3 were adults and 2 were children; all recovered from operation. The ages of the entire group of patients varied from 17 days to 72 years. Five patients were less than one year of age, 6 from 1 year to 9 years of age, 2 from 10 to 19 years of age, 3 from 20 to 29 years of age, 1 from 30 to 39 years of age, 1 from 50 to 59 years of age, 3 from 60 to 69 years of age, and 3 from 70 to 72 years of age. Thirteen patients were female and 11 were male. In 17 cases the hernia was on the right side, in 2 on the left side, in 2 it was bilateral, and in 3 cases the side was not stated. In 3 cases roentgenological examination was not done and in 1 case pulmonary cyst was diagnosed. In the 3 cases in which roentgenograms were not made, the hernia was found at necropsy. In 4 cases the roentgenological findings were confirmed at necropsy. Out of the 24 cases reported, 5 were proved by operation and 7 were proved by necropsy to be this type of hernia.

There is some difference of opinion as to whether these hernias should be classified as congenital or acquired hernias. It is impossible to explain their occurrence on a basis of faulty fusion or improper disposition of the embryonic mesodermic elements which go to form the diaphragm, as this anterior portion of the diaphragm is derived from the septum transversum only. But the consistency of the location of the hernial opening, the fairly constant relation of the neck of the sac to the round and falciform ligaments of the liver, and the frequency with which the hernial sac protrudes into the right side of the thoracic cavity at the same point of entrance at the cardiophrenic angle, as well as the often associated nonrotation of the right portion of the colon, all strongly suggest a fundamental embryologic basis for these hernias. These hernias are essentially direct hernias through a congenital defect in the structure of the diaphragm or a faulty attachment of the diaphragm to the sternum and costal cartilages. The consistency of the presence of a peritoneal sac shows that the peritoneum had closed off the abdominal cavity from the pleural cavity before the actual herniation of the abdominal viscera occurred. The consistency of the presence of the round and falciform ligaments of the liver in the peritoneum forming the sac suggests that there may be a relationship of the occurrence of this abnormal opening at the time of the rotation of the liver to the right side of the abdomen. The infrequency of traumatic lacerations involving the anterior portion or attachments of the diaphragm also supports the probability of a fundamental congenital origin of these hernias. The larger attachment of the pericardium to the anterior left side than to the right side of the thoracic diaphragm probably accounts for their increased frequency on the right side.

It is difficult to ascertain the actual incidence of subcostosternal hernias of the diaphragm, as many cases reported have not been proved by necropsy or operation. In my experience they constitute the least common type that I have operated upon. In a series of 270 operations for various types of diaphragmatic hernia, only 4 hernias were of the subcostosternal type, while 217 were through the esophageal hiatus, 14 of which were of the short esophagus type, 9 were through structural defects in the diaphragm (5 being due to congenital absence of the posterior portion of the diaphragm and 4 being of the pleuroperitoneal hiatus type) and 40 were due to traumatic lacerations of the diaphragm caused by either direct or indirect injury. In the latter group 39 were through the left side of

the diaphragm and 1 was through the right side. In the 4 cases of subcostosternal diaphragmatic hernia, the hernia extended into the right side of the thoracic cavity while in the 217 esophageal hiatus hernias only 23 extended markedly into the right side.

In the 4 cases of subcostosternal hernia, the location of the defect in the diaphragmatic muscle varied with the size of the opening. One was entirely to the right side of the midline and the 3 others were more to the right but extended beneath the sternum. In 1 of these the opening extended entirely beneath the sternum and slightly to the left of the midline, uniting the two foramina, there being no attachment of the diaphragm to the under surface of the sternum.

There was a complete hernial sac enveloping the herniated viscera in all 4 cases, and the round and falciform ligaments of the liver were involved in the peritoneal sac in all cases. The amount of involvement of the round and falciform ligaments in the formation of the sac depends on the size of the hernial sac and its extent into the thoracic cavity. In 3 of the 4 cases the sacs were very large and there was no remaining attachment of the round ligament to the anterior abdominal wall as it had been drawn entirely into the thorax and formed a part of the posterior or lateral opening of the sac.

Subcostosternal diaphragmatic hernia is one of the two types of diaphragmatic hernia, in my experience, which have a hernial sac. The other type of diaphragmatic hernia which has a hernial sac is that through the esophageal hiatus. It is interesting that subcostosternal hernia is probably the rarest type of diaphragmatic hernia and esophageal hiatus diaphragmatic hernia is the most common; both are essentially congenital in origin but are rarely present at birth and occur usually in later life because of increased abdominal pressure on a congenitally defective diaphragm.

The abdominal viscera involved in the hernias were omentum only in 2 cases, omentum and entire transverse colon in 1, and omentum, cecum, appendix, and part of ascending colon and terminal ileum in the fourth case.

The subjective symptoms in the 4 cases here reported varied from mild respiratory symptoms to repeated attacks of intestinal obstruction. In 1 case there was also an esophageal hiatus hernia which caused marked gastric symptoms. These were the patient's chief complaint, and it was not thought that the subcostosternal hernia was causing definite subjective symptoms as the omentum was the only abdominal structure involved in the hernia. This patient, a woman, also had severe asthma and it is probable that the herniation of the omentum added to her respiratory difficulty. In the second case, in which omentum only was involved in the hernia, the patient, a woman, had attacks of repeated pulmonary infections with cough and expectoration and complained of progressive dyspnea, particularly in the 2 years prior to her admission, during which time she had gained 60 pounds (27.2 kilograms). Because of the enormous amount of omentum herniated into the thorax and compressing the lung, I believe that these respiratory symptoms were due to the hernia. In both the third and the fourth case, intestine was involved in the hernial sac and the symptoms were those of periodic attacks of partial intestinal obstruction and digestive disturbance often associated with epigastric pain extending into the right side of the thorax; there were also considerable gas and bloating after meals, often associated with smothering spells and dyspnea which were more marked at night, necessitating sitting up to breathe, as well as gradually increasing constipation.

In the cases in which hollow viscera are involved in the hernia symptoms occur which suggest the possibility of a hernia or at least the necessity of a roentgenological examination of the intestinal tract which will show the presence of a hernia. The cases in which omentum only is involved in the hernia present a much more difficult clinical problem in arriving at a definite diagnosis. The subjective symptoms in the latter group are entirely thoracic as a result of mechanical interference with respiration and expansion of the lungs. These symptoms suggest a primary pulmonary lesion and direct the clinical investigation to roentgenological study of the thorax. The roentgenological findings of an increased density in the pulmonary field justify the

clinical diagnosis of a primary intrathoracic lesion which may be thought to be an intrathoracic tumor. This erroneous clinical diagnosis is particularly likely to occur if there are no subjective symptoms even to suggest that an abdominal condition may be present, and even though the gastrointestinal tract is examined roentgenologically no lesion is demonstrated as no abdominal viscera are involved in the hernia.

This, I believe, is the most important clinical consideration in this group in which the omentum is the only abdominal structure involved in the hernia. In the 2 cases here reported of this type the patients were both sent to the Mayo Clinic with a diagnosis of an intrathoracic tumor. The true diagnosis was not established until the time of the operation. In the first case there was also an esophageal hiatus hernia for which operation was advised and the subcostosternal omental hernia was found upon exploration. In the second case the true diagnosis was established by exploratory thoracotomy, although an omental subcostosternal diaphragmatic hernia was considered as a possibility before thoracotomy; however, upon roentgenological examination of the gastrointestinal tract it was found to be negative. The possibility of a subcostosternal diaphragmatic hernia was considered because of the roentgenological findings of a rounded shadow situated anteriorly, originating at the right cardiophrenic angle; the contour of the density was not completed in the thoracic cavity. I should like to emphasize the difficulties which may be associated with establishing a definite diagnosis of omental subcostosternal diaphragmatic hernia and the possibility that such a hernia may be diagnosed uncommonly as a primary intrathoracic lesion.

The treatment of subcostosternal diaphragmatic hernia is surgical closure of the abnormal opening in the diaphragm after replacement of the herniated abdominal viscera into the abdomen.

The indications for surgical intervention depend to some extent on the type of abdominal viscera involved in the hernia. In those cases in which hollow abdominal viscera are involved in the hernia, immediate surgical intervention is demanded because the danger of incarceration, obstruction, and strangulation is imminent. In cases in which it is definitely proved that the omentum is the only abdominal structure involved, operation may be delayed for reduction of weight or improvement of the patient's condition, but these patients should be carefully observed during the preoperative preparation as, with reduction in weight, the colon may be drawn into the hernial sac and immediate operation required.

The approach should be through an abdominal upper right rectus incision because the opening in the diaphragm is very accessible from the abdominal side. From the thoracic side the opening is difficult to expose as it is obscured by the right pericardial attachments to the diaphragm and access is difficult because of the contour of the right border of the pericardium which is above the opening and lateral to it.

The abdominal contents of the hernia are more safely and easily reduced from the abdominal side as the true relationship of the herniated viscera to the hernial sac can be accurately determined and any injury to these structures can be easily recognized and quickly repaired.

The treatment of the hernial sac depends on its size and on the relationship of the round and falciform ligaments of the liver to the sac. The true neck of the sac is usually to the left side of the round ligament which is pushed to the right of the midline. If the sac is small, it can be completely removed and excised and the opening in the diaphragm closed without disturbing the round ligament. If the sac is large it is best to leave it *in situ*, cut the round ligament so there will be no tendency to drag the margin of the liver up, and utilize the round ligament to strengthen the closure at the neck of the sac. If a large sac is left *in situ*, it is well to make several incisions through the peritoneum of its wall to prevent the accumulation of fluid in the sac after the neck of the sac has been closed.

The method of closure of the neck of the sac and of the defect in the structure of the muscle of the diaphragm depends on the size and character of the opening. Small linear openings may be closed by overlapping the

margins. Larger transverse openings extending beneath the sternum are best closed by suturing the anterior margin of the diaphragmatic muscle defect to the posterior sheath of the rectus muscle and anterior chest wall.

The most satisfactory material for closure of the opening is living suture of fascia lata removed from the thigh and stabilized in the tissues with silk. The round ligament of the liver can be incorporated in this closure to strengthen it as well as to re-establish its position on the anterior abdominal wall.

The closure of the large openings is facilitated by paralyzing the right side of the diaphragm by temporary interruption of the right phrenic nerve. This procedure, however, is not necessary in the closure of small openings. Preparation can be made to interrupt the phrenic nerve in the supraclavicular region after the opening is explored and it is determined whether or not interruption is necessary.

The operative approach for the repair of the subcostosternal hernia in the 4 cases which I am reporting, was abdominal in all instances. The sac was removed in 2 cases and was left *in situ* in 2. The herniated viscera were reduced and the opening was repaired in all 4 cases. There were no operative deaths and no subsequent recurrence of the hernias.

REPORT OF CASES

CASE 1. A woman, aged 64 years, consulted the Mayo Clinic on June 25, 1932, because of a diagnosis of intrathoracic tumor on the right side. Her chief complaints were asthmatic attacks with dyspnea on exertion, intermittent attacks of stomach trouble, loss of weight and strength and insomnia. With the exception of numerous irregular attacks of asthma for a period of more than 30 years, more severe in the spring and fall, she always had enjoyed good health until 4 years before her admission when she first noticed difficulty in the swallowing of food and at times she would spit up some food immediately after eating. This, however, was not associated with pain. This condition continued for about 5 months after which a roentgenogram of the stomach was taken and a diagnosis of ulcer and dilatation of the cardia of the stomach was made. Medical management for ulcer was begun, and the patient obtained complete relief of symptoms until 3 years before her admission to the clinic when following an attack of pyelitis, severe symptoms similar to the previous attack again developed. She was again relieved by medical treatment.

Three months prior to her admission to the clinic the patient had a recurrence of her digestive symptoms with spitting up of food and mucus and with epigastric distress most marked at night. Some relief was obtained from taking soda and restricting her diet to frequent small feedings. Roentgenograms of the stomach were taken again, and the patient was told that the ulcers which had been visualized at the previous examination were completely healed but that the roentgenograms of the lungs revealed an intrathoracic tumor on the right side. The patient gave no history of injury.

On physical examination her blood pressure was 128 millimeters of mercury, systolic, and 80, diastolic. Her weight was 112 pounds (50.8 kilograms). An examination of her chest showed emphysema, grade 2, on a basis of 1 to 4, and there were scattered râles of an asthmatic condition to be heard. Her fingers were clubbed, but she said this condition had always been present. Urinalysis showed an occasional pus cell, but the results were otherwise negative. The hemoglobin was 13.3 grams per 100 cubic centimeters of blood; erythrocytes numbered 4,380,000 and leucocytes 5,100 in each cubic millimeter of blood. The flocculation reaction was negative. The roentgenogram taken of the chest and stomach revealed a large tumor at the base of the right lung anteriorly, and herniation of the cardiac end of the stomach through the esophageal hiatus with a third of the stomach above the diaphragm.

Because of the preponderance of gastric symptoms, operation for the esophageal hiatus hernia was advised, and this was done on June 29, 1932, through an abdominal incision under intratracheal ethylene and ether anesthesia. Upon exploration of the abdomen, the omentum was found to pass over the dome of the left lobe of the liver and entered the right side of the thoracic cavity through an opening close to the anterior attachments of the diaphragm just to the right of the ensiform cartilage. The omentum was the only abdominal structure which passed through the opening. The transverse colon was slightly elevated but it was not involved in the hernia. It was the presence of the omentum in the right side of the thoracic cavity which produced the roentgenological shadow which was thought to be an intrathoracic tumor. The omentum was moderately adherent to the hernial sac but was removed without difficulty. The opening in the anterior surface of the diaphragm was somewhat linear, being about 3 inches (8 centimeters) in length along the costal margin, extending to the sternum, and about 1 inch (2.5 centimeters) in width. The hernial sac consisted of peritoneum and was just to the left of the round and falciform ligaments of the liver. There was a complete peritoneal sac which was about 5 inches (13 centimeters) in depth.

This sac was inverted and excised and the peritoneum was closed with the closure of the hernial opening in the structure of the diaphragm by overlapping the margins for a distance of 2 centimeters. Examination of the stomach revealed an enlarged

Fig. 1.

Fig. 3.

Fig. 4.

Fig. 5.

Fig. 1. Case 1. Subcostosternal hernia on admission. Large, rounded shadow right lower part of thorax, obscuring right border of heart and lung field.

Fig. 3. Case 1. Six months after operation. Right lung entirely expanded. Diaphragm, heart, and lung fields negative.

Fig. 4. Case 1. Herniation of cardiac end of stomach through esophageal hiatus, also on admission.

Fig. 5. Case 1. After repair of esophageal hiatus hernia, showing stomach in normal position below diaphragm. Operation performed at same time as that shown in Figure 2.

esophageal hiatus which was about 10 centimeters in diameter, through which about a third of the cardiac end of the stomach had herniated into the posterior mediastinum. The hernial sac was cut from its attachments to the stomach and permitted to retract into the posterior mediastinum. After replacement of stomach into abdomen, enlarged esophageal hiatus was repaired by overlapping from above downward; innermost suture of the repair proximal to esophagus incorporated the loose areolar tissue and remnants of peritoneal sac in the lower esophagus in the closure, fixing it to the inner margin of repaired hiatus. Stomach and duodenum did not show any intrinsic lesion (Figs. 1 to 5).

The patient's convalescence was uneventful and she was dismissed from the hospital on the twenty-first day. Her general condition was good and her wound completely healed. The roentgenogram of the stomach revealed it to be in normal position below the diaphragm and she had no gastric complaint. The roentgenogram of her lungs was normal with no evidence of the shadow in the right lower anterior portion of the chest which had been thought to be due to an intrathoracic tumor before operation.

This case is of particular interest from both a clinical and a surgical standpoint. The patient's clinical symptoms presented a dual

type of complaint. The chief complaint of loss of weight and strength and the associated asthmatic attacks with clubbing of fingers and scattered râles throughout the lungs, suggested a primary pulmonary lesion which was somewhat substantiated by the roentgenological findings of a shadow diagnosed as a tumor in the right side of the thoracic cavity. The other phase of her clinical symptoms was that of the gastric complaint which consisted of nausea, vomiting, and epigastric distress, occurring about 2 hours after meals but often noted before the patient had finished her meal. The pain was more marked at night and was relieved by belching of gas or vomiting. This phase of her complaint was fairly characteristic of an esophageal hiatus diaphragmatic hernia with an associated traumatic ulcer, as the symptoms of this condition often simulate those of a gastric ulcer.

The surgical indication in this case presented a problem as to the method of approach. I decided that the esophageal hiatus diaphragmatic hernia was responsible for the major portion of the patient's symptoms and probably for the loss of weight owing to the inability to take food. I felt, therefore, that the stomach should be explored first and that there was a possibility that the shadow in the anterior mediastinum might be an anterior type of hernia rather than a primary tumor of the lung. The discovery at operation of an esophageal hiatus diaphragmatic hernia and of anterior herniation of the omentum through the foramen of Morgagni is very unusual. In a series of 270 cases of diaphragmatic hernia in which I have operated, this is the only case in which there were two distinct congenital types of hernia through the diaphragm. This case exemplifies the importance of considering the herniation of the abdominal viscera or omentum through the diaphragm in the event of an abnormal shadow in the lower part of the thorax. I know of no other case reported in the literature which presented two separate and distinct congenital hernial openings with herniation of abdominal viscera through the diaphragm.

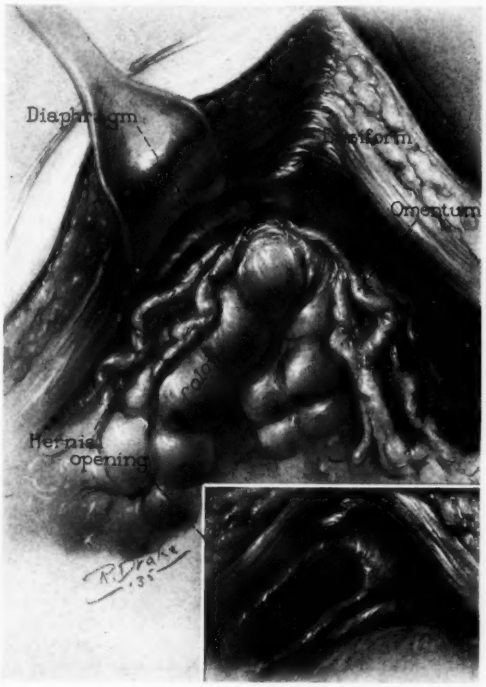


Fig. 2. Case 1. Operation by abdominal approach. Herniation of omentum and colon through opening to right of ensiform cartilage.

Case 2. A woman, aged 46 years, consulted the clinic on February 1, 1939, because of persistent productive cough of more than 2 years' duration. She had been subject to "head colds" for the past 10 years. These had become more frequent and severe since she had put on weight. She had gained 60 pounds (27.2 kilograms) in the past 2 years and on admission weighed 190 pounds (86.2 kilograms). At first there was relatively little expectoration associated with the cough, but following a severe "cold" about a year ago the patient began coughing up "greenish material that looked like pus." Since that time the cough had been productive but the sputum changed to mucoid material and amounted to about 1 cupful a day. The patient coughed mostly at night and often throughout the night and obtained some relief upon sitting up. She recently had had severe night sweats. Her voice had become husky and hoarse most of the time. Hemoptysis was not noted. She had had moderate dyspnea, more marked on exertion. Chest pain was not present. Appetite was excellent. The patient had no symptoms referable to the gastrointestinal tract. There was no history of injury. She was referred to the clinic with a clinical diagnosis of intrathoracic tumor.

On physical examination her blood pressure was 135 millimeters of mercury systolic and 85 diastolic. Examination of the thorax revealed decreased

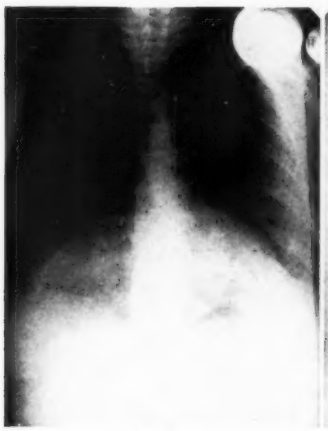


Fig. 6.

Fig. 7.

Fig. 8.

Fig. 6. Case 2. Anteroposterior view on admission. Dense rounded tumor right lower part of thorax. Preoperative diagnosis was benign tumor or encysted fluid.

Fig. 7. Case 2. Lateral view on admission. Shows that dense rounded tumor is located anteriorly, completely obscuring heart shadow.

Fig. 8. Case 2. On admission. Entire colon in normal position below diaphragm.

fremitus, diminished breath sounds and dullness to percussion over the lower area of the right lung. Urinalysis showed pus, grade 1, but the results were otherwise negative. The hemoglobin was 13.8. grams per 100 cubic centimeters of blood and leucocytes numbered 7,400 in each cubic millimeter of blood. Flocculation reaction was negative. X-ray examination of thorax showed a homogeneous opacity over lower and anterior fields of right lung, thought to be a benign tumor or encysted fluid (Figs. 6, 7).

Although there were no abdominal symptoms, the position of the shadow in the right side of the thoracic cavity originating at the cardiophrenic angle anteriorly suggested the possibility of a subcostosternal hernia, and the entire gastrointestinal tract was examined roentgenologically but found to be normal (Fig. 8). The clinical diagnosis was intrathoracic lesion, probably tumor, and exploration was advised.

A right artificial pneumothorax was done preliminary to the operation and roentgenograms taken after this procedure did not give any additional information as to the lesion. The transpleural exploration of the right side of the thoracic cavity was carried out on February 15, 1939. The seventh rib was resected and upon exploration of the thorax a large tumor mass was found originating from the right cardiophrenic angle of the lower right side of the thoracic cavity and extending entirely behind the mediastinal and anterior parietal pleura to the hilum of the right lung superiorly and to the midportion of the right side of the thoracic cavity laterally. This anterior mass occupied a third of the entire right side of the thoracic cavity, compressing the lower and middle lobes of right lung posteriorly. The pressure had produced adhesions between the parietal and visceral pleura around the mass.

After separation of these adhesions and section of the pleura the mass was found to be a peritoneal hernial sac coming through an opening in the anterior portion of the diaphragm just beneath the costosternal junction. The peritoneal sac was opened and was found to contain an enormous omental fat apron. It was impossible to replace this herniated omentum through the relatively small hernial orifice owing to the fixation of the omentum at the neck of the sac which was angulated beneath the right border of the heart. It is possible that replacement might have been accomplished by enlarging the opening in the diaphragm, but I did not think this procedure was advisable, as the patient was very obese and there was no space in the abdominal cavity to receive this huge omental mass. I did not think it advisable to enlarge the opening because of the danger of injury to the colon, and it was thought best to close the thoracic cavity as an exploration and to replace the herniated omentum through an abdominal approach at a later operation after the patient's weight had been reduced.

The patient made a good recovery from the exploratory thoracotomy and was permitted to return home on a reduction diet. She returned to the clinic in 3 months, having lost 50 pounds (22.7 kilograms). Her general condition was very satisfactory. On June 17, 1939, the right subcostosternal hernia was repaired under cyclopropane anesthesia, through an upper right rectus abdominal approach.

On exploration of the abdomen a relatively large subcostosternal opening through the right anterior portion of the diaphragm was found. The opening was mostly on the right side but also extended beneath the sternum and slightly to the left of the midline. It was somewhat kidney-shaped because the

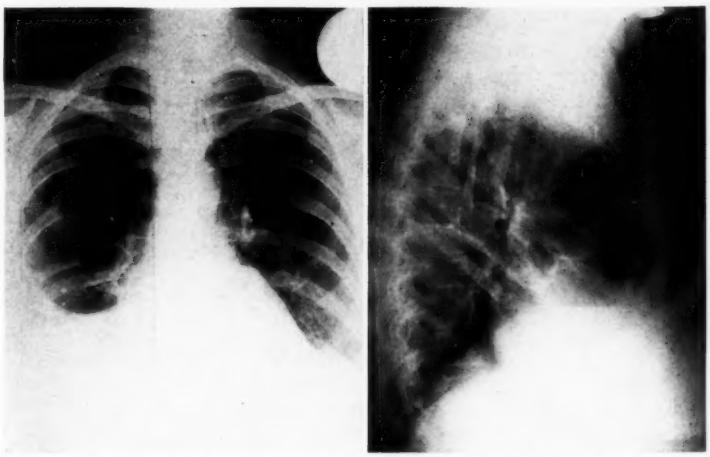


Fig. 9, left. Case 2. Anteroposterior view. After repair of subcostosternal hernia. Lung almost completely expanded. Small amount of fluid in residual sac.
Fig. 10. Case 2. Lateral view after repair of hernia.

falciform and round ligaments of the liver were contained in the hernial sac posteriorly. The hernial sac consisted of peritoneum; the neck of the peritoneal hernial sac extended into the thorax and was angulated upward and forward. The peritoneal opening was to the right of the midline but to the left of the round and falciform ligaments of the liver. There was a depression in the peritoneum to the right of the round ligament, but it was impossible to pass a finger into the hernial sac to the right of this ligament. The entire omentum had herniated through this opening and was quite adherent to the margins of the opening of the sac.

The omentum was entirely separated from its attachment to the neck and from the sac itself and replaced into the abdomen. The falciform and round ligaments were then cut away from their attachments to the hernial sac so as to sever their continuity with the sac and permit a more accurate closure of the neck of the sac. Because of the huge size of the sac, which extended high into the thoracic cavity, and its known fixation to the lung, no attempt was made to remove the entire sac. Several incisions were made into the wall of the sac to prevent accumulations of fluid in the sac. The hernial orifice and neck of the sac were then closed by overlapping the left side over the right side for at least 1.5 to 2 centimeters. The closure was made with a continuous suture of fascia lata which had been removed from the right thigh and the fascia was fixed into this overlapped closure with interrupted linen sutures. The cut round and falciform ligaments were then sutured over this closure to reinforce it as well as to re-establish normal position of round ligament to its attachment to abdominal wall and aid in obliterating this space above liver to prevent entrance of abdominal viscera to this region.

A transfusion of blood was given immediately after the operation. The patient's convalescence was uneventful. The patient was dismissed from our care about 4 weeks from the time of operation, at which time the wound was entirely healed. Her general condition was very satisfactory. The roentgenogram of the thorax revealed that the hernial sac was obliterated completely. There was still increased density over the right lower part of the thorax from thickened pleura resulting from the previous thoracotomy wound (Figs. 9 and 10). The patient returned to the clinic for a recheck of her condition 1 year after repair of hernia. She was in excellent health and had no subjective symptoms. The roentgenograms revealed small interlobar pleuritic bands in right lower thorax. The lung fields were normal. There was no recurrence of the hernia.

This case is interesting because of the difficulties encountered in establishing a clinical diagnosis, which resulted in the necessity of two operative procedures in order to effect a cure of the condition. Although the possibility of a subcostosternal hernia was suspected, this preoperative diagnosis could not be established. The entire gastrointestinal tract was examined roentgenologically before operation and it was found that the stomach and the colon were in normal position and there was no evidence of any deviation from their normal position to suggest herniation of these viscera or of the omentum. Inasmuch as one of the patient's subjective symptoms suggested an intrapulmonary or intrathoracic

lesion, and as this suggestion was substantiated by clinical and roentgenological findings, exploratory thoracotomy was indicated.

The case is also of interest because of the difficulty encountered in attempting to replace the herniated omentum from the thoracic approach. Two courses could have been followed. The omentum could have been excised and the opening in the diaphragm could have been enlarged but because of the extreme obesity of the patient and the fact that the omentum had lost its right of residence in the abdomen as well as the possibility of injury to the colon, these procedures were not thought advisable. A certain hazard was taken in permitting the patient to return home because of the possibility of the colon becoming involved in the hernia, particularly following reduction in weight and decrease in the fatty omental content of the hernial sac, as the only reason that the colon had not become involved in the hernia was that the sac was completely filled with omentum. The patient was cautioned on her first dismissal that if she experienced any abdominal symptoms she should return for operation without any further delay. The ultimate satisfactory result obtained from the abdominal reduction and repair of the hernia was very gratifying.

CASE 3. A man, aged 27 years, consulted the clinic on June 6, 1940, because of irregular periodic attacks of abdominal distress and bloating of 7 years' duration. He stated that he had always been in excellent health until the onset of these symptoms. He first noticed that his abdomen would become distended after meals. This distention was associated with generalized abdominal distress which had recently reached a degree of severe pain. The pain was most severe when he lay down at night. On several occasions he had had a smothering sensation which would be relieved by sitting up. He would have nausea following meals but had never vomited. He had noticed gurgling in the abdomen which would extend into the lower part of the chest. He had become increasingly more constipated, requiring the constant use of laxatives. His general condition had remained satisfactory except for weakness and loss of weight. There had been no history of injury.

On physical examination the patient was found to weigh 116 pounds (52.6 kilograms). His normal weight was 138 pounds (62.6 kilograms). The loss of weight extended over a period of 7 years. Examination of the abdomen revealed slight generalized tenderness. Examination of the chest revealed a percussion note under the sternum, rather tympanic. The blood pressure was 152 millimeters of mercury systolic and 80 diastolic. Urinalysis revealed an occasional erythrocyte and an occasional pus cell, but the results were otherwise negative. The hemoglobin was 14.4 grams per 100 cubic centimeters of blood; erythrocytes numbered 5,160,000, and leucocytes 7,300 in each cubic millimeter of blood. The flocculation reaction was negative. The roentgenological examination of the thorax was reported as giving negative results. The roentgenological examination of the colon revealed herniation of the cecum and ascending colon as well as a portion of the terminal ileum through an opening in the anterior right side of the diaphragm with the aforementioned portions of the bowel lying in the anterior mediastinum slightly to the right of the midline and just to the right and posterior to the lower part of the sternum and the xiphoid process (Figs. 11 and 12). The fluoroscopic examination of the diaphragm showed the motion of both sides of the diaphragm to be equal and normal.

A clinical diagnosis of a right subcostosternal diaphragmatic hernia was made and temporary interruption of right phrenic nerve followed by abdominal repair of hernia was done June 19, 1940.

Temporary interruption of the right phrenic nerve by crushing the nerve was done through a right supraclavicular incision. The abdomen was then explored through an abdominal right rectus incision under cyclopropane anesthesia. The ileocecal coil was found to extend over the left lobe of the liver and through an opening in the right anterior part of the diaphragm. There was also herniation of a portion of the omentum. These structures were moderately adherent but were removed without difficulty and were dropped back into the abdomen. After removal of the herniated viscera, the defect in the anterior right part of the diaphragm could be visualized. This opening was chiefly in the right side of the diaphragm but extended beneath the sternum. The portion of the opening to the right corresponded to the foramen of Morgagni. There also had been a lack of fixation of the diaphragm to the lower end of the sternum. The opening was about 6 centimeters in length along the costosternal attachment and it was about 4 centimeters in width. There was a complete hernial sac consisting of peritoneum of the diaphragm and anterior abdominal wall. This sac extended into the thoracic cavity for about 8 to 10 centimeters. The round ligament of the liver extended with the hernial sac into the thoracic cavity and the opening was to the left of the round ligament. The left lobe of the liver was very much smaller than normal and was rounded in contour. The right lobe was about normal in size and shape.

The hernial sac was removed from the thoracic cavity and partially excised, and the margins of the defect in the diaphragm were closed by overlapping and fixing the diaphragm to the chest wall with two sutures of continuous fascia lata removed from the right thigh. The round ligament, which had been cut from its attachment to the sac, was then incor-

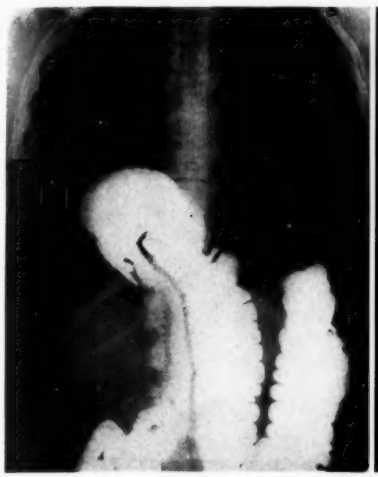


Fig. 11.

Fig. 12.

Fig. 13.

Fig. 11. Case 3. Anteroposterior view on admission. Subcostosternal diaphragmatic hernia (foramen of Morgagni) with herniation of ileocecal coil into right side of thoracic cavity.

Fig. 12. Case 3. Lateral view on admission. Shows ileocecal coil herniated through an opening in anterior portion of diaphragm.

Fig. 13. Case 3. Five weeks after repair of hernia. Ileocecal coil in normal position in right lower quadrant of abdomen.

porated into the closure and fixed to the anterior chest wall. The fascia lata was fixed in the tissue with interrupted silk sutures. Although there was nonrotation of the cecum, it had a relatively long mesentery. The appendix was retrocecal and showed evidence of chronic inflammation; therefore, appendectomy was done. No attempt was made to fix the cecum in its normal position in the right lower quadrant of the abdomen. The abdomen was closed.

The patient was immediately placed in an oxygen tent where he remained until the third postoperative day. His postoperative course was without incident. He was dismissed from the hospital on the seventeenth postoperative day and from our care one week later. At that time the wound was entirely healed and he was feeling very well generally. The roentgenogram of the colon showed it to be in normal position with the cecum in the right lower quadrant of the abdomen (Fig. 13).

This patient presented the subjective symptoms to be expected in cases in which a part of the intestinal tract is involved in the hernia. These symptoms are those of intermittent intestinal obstruction. In this instance the obstruction was partial; however, this could become complete at any time. The most interesting consideration in this case is the portion of the intestinal tract which was involved in the hernia; namely, the cecum, appendix, ascending colon, and terminal ileum.

It is interesting to speculate at what time in life this hernia occurred. It was quite evident that there was nonrotation of the colon, as this portion of the bowel is very unlikely to herniate through the anterior portion of the diaphragm after the cecum has once attained its normal position in the right lower quadrant of the abdomen. The nonrotation of the colon would indicate that this hernia may be of congenital origin, although it is difficult to understand why the symptoms had not been present until about the patient's twentieth year of age if the nonrotated ileocecal coil had been in the hernia since birth. The possible congenital origin of this hernia is also suggested by the fact that the ileocecal coil, upon being released from the hernial opening, very soon attained its normal position in the right lower quadrant of the abdomen as shown by the roentgenogram of the colon taken 3 weeks after operation. That this normal position of the cecum was attained by the intestine although no attempt at mechanical fixation of it in this position was made at the time of operation indicates that the bowel had never had a previous opportunity to attain its normal position.

Fig. 14, left. Case 4. Anteroposterior view on admission. Subcostosternal diaphragmatic hernia with herniation of large portion of transverse colon into right side of thorax.
Fig. 15. Case 4. Lateral view, on admission, shows that colon has herniated through an opening in anterior portion of diaphragm.

CASE 4. A man, aged 34 years, consulted the clinic on March 24, 1937, because of repeated attacks of gas and belching with severe pain in the chest. He stated that 2 years prior to his admission he had had an attack of sharp pain in the right upper quadrant of the abdomen which lasted for 5 days, following which he had considerable gastric distress. Three months later he had a severe attack of gas and belching with severe pain in the chest and over the heart after he had eaten "hamburger" and drunk beer. He could not lie down and morphine was required for relief. One week later he had a similar attack. Since this attack he had to take something to make his food digest. His appetite was good. Immediately after meals and occasionally between meals he would have a sensation of rumbling and rolling of gas in his chest. During some of these attacks he had pain in the right epigastrium and near the right shoulder blade. This pain might occur with or without relation to meals. Recently even a glass of water would make the stomach feel full. Although the patient became nauseated after meals he had never vomited. There had been no history of injury.

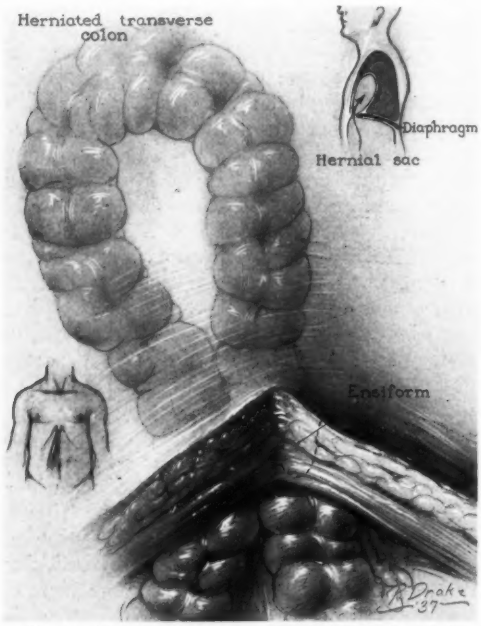


Fig. 16. Case 4. Entire transverse colon and omentum herniated through a large subcostosternal opening (foramen of Morgagni), right of midline.

On physical examination the patient was found to be well developed and well nourished. His weight was 160 pounds (72.6 kilograms). Examination of the abdomen revealed tenderness in the epigastrium and right lower quadrant. The blood pressure was 124 milligrams of mercury systolic and 80 diastolic. The results of urinalysis were negative. The hemoglobin was 18.5 grams per 100 cubic centimeters of blood; erythrocytes numbered 4,970,000 and leucocytes 11,500 in each cubic millimeter of blood. The flocculation reaction was negative.

Roentgenograms of the chest revealed a circumscribed shadow in the right cardiophrenic angle above the right side of the diaphragm. A diaphragmatic hernia was suspected. The roentgenogram of the stomach showed it to be in normal position. The roentgenogram of the colon revealed

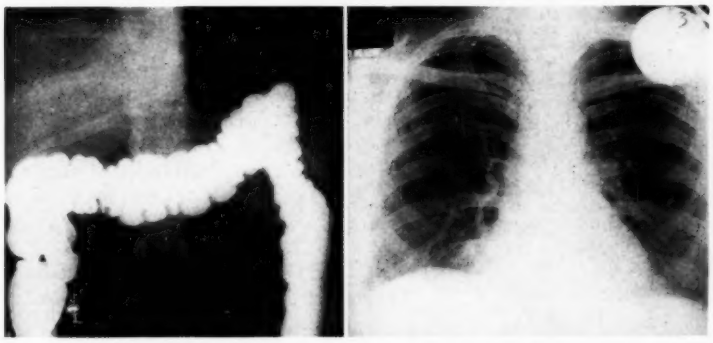


Fig. 17, left. Case 4. On dismissal. Colon in normal position below diaphragm.
Fig. 18. Case 4. One year after repair of subcostosternal hernia. Pleuritic adhesions right costophrenic angle. Lung fields negative.

herniation of a large portion of the transverse colon into the right side of the thoracic cavity, through an opening in the anterior part of the diaphragm (Figs. 14 and 15). The colon extended to the level of the second rib anteriorly. A diagnosis of subcostosternal diaphragmatic hernia with herniation of the transverse colon into the right side of the thoracic cavity was made.

Operation was performed on March 31, 1937, under cyclopropane anesthesia through an upper right rectus abdominal approach. On exploration of the abdomen it was found that the omentum and entire transverse colon had herniated through an opening in the anterior part of the diaphragm which was beneath the sternum, extending mostly to the right side but partly to the left side of the sternum. The opening measured about 10 centimeters in diameter and extended across the entire anterior portion of the chest wall. The colon and omentum were moderately adherent to the peritoneal sac which extended to the second rib anteriorly in the right side of the thoracic cavity (Figs. 16 and 19).

After removal of the colon and the omentum from the opening, it was found that there was a complete hernial sac of peritoneum which was a continuation of the peritoneum of the diaphragm and anterior abdominal wall. After removal of the herniated abdominal viscera, there was marked suction through the hernial opening, but this was due to the suction of air into the hernial sac as there was no direct communication with the pleural cavity. The round ligament of the liver was incorporated in the portion which formed the hernial sac and extended into the thoracic cavity. Both the round and falciform ligaments were pulled out of the thoracic cavity, but it was impossible to remove the hernial sac because of its firm attachment to the thoracic viscera and chest wall, high in the thoracic cavity. The round ligament of the liver was cut and the end distal to the liver, which had been attached to the abdominal wall, was permitted to retract into the thorax with the hernial sac (Figs. 20 and 21, frontispiece). Linear incisions were made into the sac to permit fluid to drain out after closure of neck of hernial sac. The opening was closed by suturing it to the posterior sheath of the rectus muscle on both sides. The tissues were first stabilized with silk, and then living sutures of fascia lata,

Fig. 19. Case 4. Hernial sac of peritoneum and pleura, anterior right portion of thorax, containing herniated transverse colon and omentum, compressing right lung.

which had been removed from the right thigh, were interwoven between the layers of the closure.

The patient was immediately placed in an oxygen tent; however, his convalescence was complicated by bronchopneumonia. He was very ill for the first 5 days. We were able to remove him from the oxygen tent on the tenth day and his convalescence from that time was satisfactory except for drainage from the wound resulting from partial separation of the wound due to coughing. Roentgenograms of colon 5 weeks after operation showed it to be in normal position below diaphragm (Fig. 17). Patient dismissed from our care 6 weeks after operation. He returned for observation 1 year following operation, when the roentgenogram revealed the colon well below the diaphragm (Fig. 18). There was no evidence of intrinsic lesion of the colon. The roentgenogram of the chest revealed pleuritic adhesions at the right costophrenic angle.

The subjective symptoms presented by this patient indicated very severe attacks of obstruction bordering on complete obstruction. Considering the huge size of this hernia and the large amount of colon extending into the thoracic cavity through a relatively small opening, it is remarkable that acute complete obstruction did not develop. This was the largest of the 4 hernias of this type which I have operated upon. The colon extended to the second rib anteriorly. There was dilatation of the proximal colon, indicating that there had been considerable obstruction. This is the only one of the 4 cases in which any serious postoperative complications developed. It is possible that the amount of compression causing atelectasis of the lung may have been a factor in the postoperative pulmonary complication which prolonged convalescence.

SUMMARY

Subcostosternal diaphragmatic hernia is a relatively rare type of hernia; there were only 4 in a series of 270 cases of various types of diaphragmatic hernia in which I have operated.

A complete report of the clinical manifestations, surgical indications, and operative procedures has been given of these 4 cases. All 4 patients were adults and there was no history of injury in any of the 4 cases.

Two patients were women, 64 and 46 years of age, and 2 patients were men, 34 and 27 years of age. (One patient, a woman, aged 64 years, had an esophageal hiatus diaphragmatic hernia as well as a subcostosternal hernia. I know of no other similar case of double diaphragmatic hernia in the literature.)

In all 4 cases a complete hernial sac projected into the right thoracic cavity.

The contents of the hernial sac were omentum only in 2 cases, in both of which the patient was a woman; these patients presented pulmonary symptoms only and the lesion was diagnosed clinically and roentgenologically as a primary intrathoracic lesion, the results of examination of the gastroenterological tract being negative. The difficulty of establishing a definite clinical diagnosis by clinical symptoms, physical examination or roentgenographic findings, is of the utmost importance in the clinical consideration of these omental hernias. In one case an exploratory thoracotomy was performed before the diagnosis was established. At this time it was impossible to reduce the hernia which was repaired later by abdominal approach. The omental subcostosternal hernia was found and repaired in the other case at the time of repair of the esophageal hiatus hernia. This was an unusual case presenting 2 congenital hernias of different types. The contents of the sac in the third and fourth cases, in both of which the patients were men were omentum and transverse colon, and omentum, terminal ileum and cecum, respectively. These patients presented the usual symptoms of intermittent digestive disturbances and partial intestinal obstruction.

The surgical approach for repair of the subcostosternal hernias was through a right rectus abdominal incision in all 4 cases, and the defect in the diaphragm was closed with living suture of fascia lata stabilized with silk sutures.

The hernial sac was excised in 2 cases and left *in situ* in 2 cases. There were no operative deaths and there have been no recurrences.

CEREBRAL ARTERIOVENOUS ANEURYSMS

BRONSON S. RAY, M.D., New York, New York

DIRECT communication between the arterial and venous systems of the body exists either as an acquired lesion due to trauma or disease, or as a developmental anomaly. Abnormal communications between intracranial vessels external to the brain occur chiefly between the internal carotid artery and the cavernous sinus. These extracerebral lesions arise spontaneously in diseased vessels or, as more frequently happens, they result from trauma. Their formation is dependent upon an anatomical arrangement that has no analogy elsewhere in the body. But abnormal communications between the pial and cerebral arteries and veins are probably always congenital, and it is this latter type of lesion with which the present study is concerned.

The arteriovenous communications of the brain in the past have been variously designated. Cushing and Bailey (3) in their monograph, *Tumors Arising from the Blood Vessels of the Brain* (1928), which was the first noteworthy attempt at clarification of the subject, referred to these lesions as angioma arteriole. They listed the following synonyms: angioma plexiforme or anastomoticum, varix arteriole or aneurysmaticus, Rankenangiom or Rankenaneurysm, angioma varicosum or cirsoides, and hemangioma racemosum arteriole et venosum. Synonyms used by others have been: angioma cavernosum, varix aneurysmaticus, aneurysma serpantina, aneurysm anastomatica. Dandy (1928) chose to call the lesions simply arteriovenous aneurysms. The latter term is perhaps the most useful, principally because it leaves no doubt about the nature of the lesion.

The reports of about 75 cases have accumulated in the literature, and there has been considerable variation and some misunderstanding in regard to the nature of the lesion, the interpretation of its clinical manifestations, and the possibilities for treatment. Personal experience with a group of 6 cases having arteriovenous aneurysms of the brain in which careful investigations have been made and the progress observed after a variety of therapeutic measures, has prompted this reconsideration of the subject.

From the Department of Surgery of The New York Hospital and Cornell University Medical College.

CASE 1. Frequent headaches since the age of 4, and infrequent convulsive seizures since the age of 26 in a 41 year old man. Slight increase in intracranial pressure and calcified areas in the left frontal lobe. Cephalic bruit, not discovered before operation. Distortion of the ventricles seen by ventriculography. Arteriovenous aneurysm of the left frontoparietal area of brain disclosed by osteoplastic operation. Subtemporal decompression. Improvement in headaches and convulsions 4 years later.

On July 24, 1936, Frank B., aged 41, a plasterer, referred by Dr. Edward M. Livingston of New York City, was admitted to the hospital, complaining of headaches and convulsive seizures.

At the age of 4 years the patient was critically ill in Italy with what was thought to be typhoid fever. After recovery from this illness he began shortly to experience periodic headaches which occurred every 3 to 4 weeks. These headaches were dull and usually bifrontal, occasionally associated with vomiting, and lasted on an average of 8 hours. They continued to recur through the years and, although he was sometimes confined to bed with them, he usually found sufficient relief from aspirin to continue his activities.

Three years before admission a new type of headache replaced the old one. This headache appeared almost daily and events associated with it followed a definite pattern. He would first experience a "burning sensation in the pit of the stomach" followed within a few minutes by a pain in the left supraclavicular region which, within the next 10 to 20 minutes, gradually traveled up the left side of his neck to the face, then "swept over the left side of the head" and centered in the left forehead as a violent throbbing pain. This would be associated with a watering of the left eye and temporary haziness in the vision of that eye. Ten grains of aspirin taken with the onset of the pain would give him relief within 20 to 30 minutes. He was unable to relate the onset of these headaches to any known incident.

He had his first convulsive seizure at the age of 26 (15 years before admission), and had about 1 a year thereafter. Three attacks occurred at night while he was asleep and one occurred while he was sitting quietly; all the others occurred during the activity of his waking hours. With the onset of an attack he felt a "quivering in the stomach" (unlike the sensation preceding headache) and this was followed by

an uncontrolled cry and loss of consciousness. The attacks were always generalized according to the account given and lasted 20 to 40 minutes. There was no relationship between headaches and the convulsions, and at the termination of a convulsion he felt only extreme fatigue and had no local palsies or paresthesias.

His general physical condition was not remarkable: his intelligence and mental attributes were above average. There were no nevi or abnormal pigmentations over the body. The blood pressure was 118/70, the cardiac rate was 70 and the radial pulse was of normal character. There were a few prominent pulsating vessels in the left frontotemporal region, but the great vessels of the neck were not abnormally pulsatile and no bruit was discovered over the head or neck prior to operation. There was a definite bilateral papilledema of less than one diopter, greater on the left. The retinal vessels, both arteries and veins, were full and tortuous and difficult to distinguish from each other. Visual fields and acuity were normal. Quantitive smell-function on the left was one-third that on the right. Other functions of the head were normal as were motility and sensory functions and reflexes over the body.

Blood and urine tests were normal. The spinal fluid was under moderate increase in pressure (220 mm. of water) and the total protein was .050 grams per cent.

Roentgenograms of the head showed the cranium to be of normal size, shape, and thickness. The frontal sinuses were of medium and equal size. There was very slight accentuation of the convolutional markings of the skull, and the posterior clinoid processes were atrophic. One or two local areas of rarefaction appeared to be the result possibly of pressure from the vessels of the aneurysm. The vascular markings (diploe) were accentuated, particularly on the left in front and near the vertex. There was increase in the size of the groove for the middle meningeal artery on the left as compared to the right; the foramen spinosum was not well demonstrated. The pineal was calcified and in normal position. There was spotty calcification in left frontoparietal region at a site corresponding to precentral area of cortex. There was also calcification in intracranial segment of left internal carotid artery.

A diagnosis of tumor, probably meningioma, of the left frontal cerebral lobe was presumed.

Ventriculography was performed, July 27, 1936. Thirty cubic centimeters of clear fluid, found under moderate increase in pressure, were exchanged for air. The roentgenograms showed normal sized ventricles, but a slight shift of the lateral and third ventricles to the right and a slight depression of the left frontal horn (Figs. 1a and b).

Operation was done July 30, 1936. After ether anesthesia had been administered, a left parietal osteoplastic operation was performed (Fig. 2). Neither the scalp nor the bone appeared unduly vascular but upon elevation of the bone from the dura, enlarged and tortuous middle meningeal arteries tore easily and bled briskly. As the dura was reflected from the brain, large tortuous and intertwined vessels were revealed in the upper part of the prerolandic area. These vessels were obviously large veins but were tense, pulsating, and had an arterial color. They appeared to extend on up to the sagittal sinus and downward into the lateral cerebral fissure but in this latter direction they were smaller. Elsewhere over the exposed frontal lobe all cortical vessels were several times larger than normal and even those that could be distinguished as veins had a reddish arterial color. In addition, there were several stubby vessels, 2 to 3 millimeters in diameter, connecting these cortical vessels and the dural arteries. No attempt was made to ligate any of the vessels except those communicating with the dura. A fair sized decompression was created beneath the temporal muscle and the bone flap was replaced and sutured.

The recovery from operation was prompt and the only complication was a transitory aphasia which disappeared by the twelfth postoperative day. The headaches were greatly improved. A bruit was heard faintly on auscultation over the left parietal area near the midline and could easily be overlooked if it were not anticipated. The bruit was quite distinct over the area of decompression but it was not heard elsewhere over the head. It was faintly heard over the left eyeball and left carotid artery in the neck. The patient was not aware of noises in the head at any time. Compression of the left common carotid artery caused slight diminution in the bruit; of both carotids, almost complete obliteration of the bruit.

After operation, 1050 r units of roentgenotherapy were administered in 10 doses. The decompression though slightly full was not tense. There was no essential change in the appearance of the optic fundi.

The patient was seen at regular intervals in the 4 years after operation. Two additional series of roentgenotherapy, each of 1,000 r units, were given during first 6 months but patient refused more.

He was greatly relieved of his headaches for a year after operation. After that he again began to have daily left frontal headaches but of much less severity than before operation. These headaches were unaccompanied by the former pain in the left shoulder, neck, and face. He took no medication except aspirin and had but one mild convulsion (September, 1938).

No new physical signs developed. The bruit remained the same. The decompression varied in its fullness but the optic disks remained slightly full.

Headache was the complaint that finally brought this patient to the hospital. It had first appeared at the age of 4 years and is fairly good evidence that his vascular lesion was present early in life. The headache of later years had many of the aspects of migraine by its involvement of one side of the neck, face, and head; at least it was characteristic of pain of vascular origin. Since the large

Fig. 1a. Case 1. Ventriculogram showing deformity of the body and frontal horn of the left lateral ventricle.

cerebral vessels were the most conspicuous feature of this man's lesion it might be supposed that dilatation of these vessels was directly responsible for at least the pain in the head, but since the normal pial vessels over the cerebral convexity are not pain sensitive this explanation is improbable (20). A more reasonable explanation for the headache would be the distention of the pain sensitive dural arteries which in this individual were seen not only to be enlarged but also in direct communication with the large vessels of the aneurysm. Transection of the middle meningeal artery low in the temporal region interrupted both the proximal blood supply and the nerve supply to the distal portions of that artery. This alone is sufficient to cause improvement in headache (9). The partial return of headache a year or so later might well result from return of nerve supply to the dural arteries.

Slightly increased intracranial pressure was evidenced by the low grade papilledema. In all probability there had been fluctuations of intracranial pressure in the past. The lack of fullness of the decompression except for the first several days after operation demonstrated the absence of marked or sustained elevation of pressure. The decompression and the interruption of the middle meningeal artery doubtless each deserve some of the credit for the improvement in patient's headaches and the diminution in the frequency of convulsions.

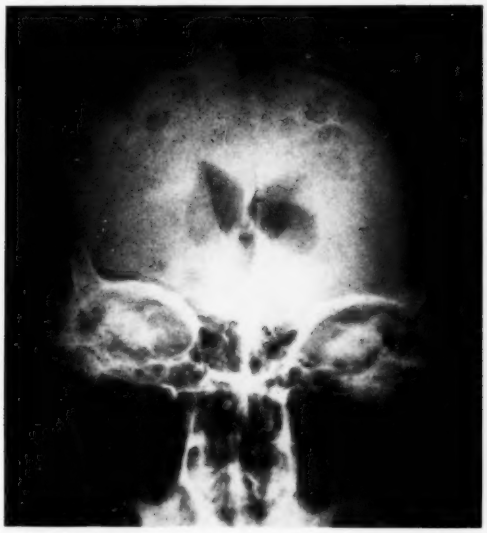


Fig. 1b. Case 1. Ventriculogram showing depression of the lateral ventricle on the left side.

CASE 2. Occasional paresthesias and convulsive movements in left upper extremity for 3 years and mild schizoid psychosis for 6 months in woman, aged 43. Arterial hypertension and slight left hemiparesis. Cephalic bruit, not discovered before operation. Distortion of the ventricles seen by ventriculography. Arteriovenous aneurysm of right parietal area of brain disclosed by osteoplastic exploration. Subtemporal decompression. Roentgenotherapy. Diminution in frequency and severity of convulsions but increase in psychosis 4 years later.

On September 1, 1936, Helen R., aged 43, an unmarried grade school teacher, referred by the Rockefeller Institute and the Payne Whitney Psychiatric Clinic of New York City was admitted to hospital, complaining of attacks of numbness and weakness in the left hand and arm.

Until 3 years before admission she had been in good health and without complaint. At the age of 40 she began to experience periodic sensations of a "numb, cold, dead feeling" in the left hand and arm which sometimes spread over the entire left side of the body. The attacks occurred at first about once a month but later as often as several times a week and lasted from 1 to 15 minutes. At the age of 41 the attacks of paresthesia became associated sometimes with an uncontrolled tonic contraction of the left hand and arm. During the year before admission to the hospital she lost consciousness several times in the course of these attacks but never had a generalized convulsion.

A typical attack was ushered in usually by a sensation of pounding in her ears, a "rushing of blood to the head" and a "beating sensation all over the

Fig. 2. Case 2. Drawing made from postoperative sketch giving site and general appearance of the lesion. Note abnormal vessels anastomosing the lesion and the middle meningeal artery.

body." She had no tinnitus between attacks and never had headache at any time.

A year prior to admission she was found to have unexplained hypertension. Examination showed slight enlargement of the heart to the left and electrocardiographic changes indicating left ventricular preponderance, but no renal pathology.

During the 6 months prior to admission she developed distinct changes in mood, was overly suspicious of people, and had hallucinations of hearing voices. A sister had committed suicide during a state of depression. After the patient had been observed at the psychiatric clinic, a diagnosis was made of "paranoid reaction with panic episodes"; the prognosis was thought to be serious. It was while she was being observed in this clinic that a left sided convulsive seizure was seen by a physician for first time.

Examination disclosed no papilledema but the vessels of the right retina were full and tortuous; the veins were of a lighter color than usual. Visual acuity and perimetry were normal. There was very slight weakness of the left lower face and of the left upper extremity. There were no sensory changes. The deep reflexes in the left upper and lower extremities were increased but the superficial reflexes were normal. The blood pressure at rest averaged 165/108 and the cardiac rate averaged 80. The pulse had a bounding quality. The heart was normal on physical examination although it was shown to be slightly enlarged to the left by roentgenography.

Laboratory studies of the blood and urine showed normal values.

Roentgenograms of the head (Figs. 3a and b) showed the cranium to be of normal size, shape, and thickness. The frontal sinuses were of moderate and equal size. There was very slight accentuation of the convolutional markings of the skull and the posterior clinoid processes were thin but there was no frank evidence of increased intracranial pressure. There were one or two areas of rarefaction of the inner table of the right parietal bone, possibly the imprint of vessels of the aneurysm. The vascular markings (diploe) were accentuated over the entire skull and in the parietal regions there were the markings of large venous lakes. The groove for the right middle meningeal artery was increased in size although there was no change in the size of the foramen spinosum. There were no intracranial calcifications except in the falx cerebri.

A diagnosis of right frontoparietal neoplasm was presumed.

Ventriculography was carried out on September 1, 1936. The ventricular fluid was found to be clear and under slightly increased tension. Twenty cubic centimeters of fluid were removed and exchanged for air. Roentgenograms showed normal sized ventricles with no lateral shift, but the superior wall of the body of the right lateral ventricle had a serrated appearance as from the projection of nodular lesions into the ventricle.

Operation was performed September 1, 1936. After ether anesthesia had been administered, a right parietal osteoplastic operation was performed. Neither the scalp nor the bone was unduly vascular, and the dura was not adherent to the bone. The middle meningeal artery, however, was about twice the expected size and bled vigorously when cut. When the dura was reflected a number of tortuous vessels, some as large around as a lead pencil or larger, were seen to overlie the precentral area almost completely obscuring the cortex. Tense and tortuous vessels of smaller caliber and less closely arranged were present over the rest of the exposed area. Bright red blood was seen swirling through the larger vessels and a thrill was felt on palpating them. There were no normal looking arteries or veins in the exposed field. Three short but wide vessels passed directly from one of the cortical vessels to the dura and were seen to anastomose with dural arteries; these were clipped and cut. A fairly large subtemporal decompression was made and wound closed.

Recovery from operation was uncomplicated. The bruit, which had not been discovered before operation, was distinct but of low intensity over the right frontoparietal region, over the right eyeball, and over the right carotid artery in the neck. The patient herself was never aware of the bruit even when it was suggested that she might hear it. Compression of the right carotid artery diminished the intensity of the bruit about half. The decompression was never found to be tense during the recovery period. Roentgenotherapy totaling 1,100 r units was administered within 2 weeks after operation had been performed.

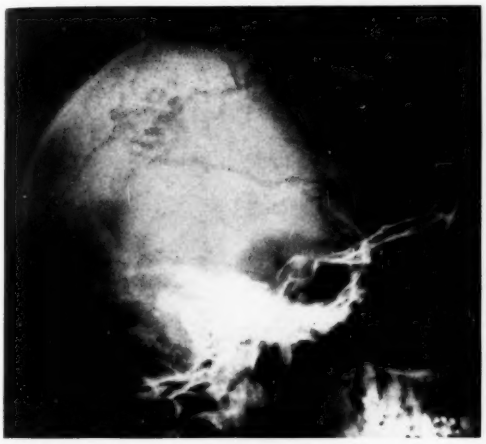


Fig. 3a. Case 2. Lateral roentgenogram of the skull showing accentuation of the diploic channels.

Fig. 3b. Case 2. Posteroanterior roentgenogram of the skull showing accentuation of diploic channels.

Repeated series of roentgenotherapy were administered over the next 18 months until a total of 10,200 r units had been given. The patient had rare attacks of uncontrolled clonic contractions in the left upper extremity in the 4 years after operation. There was no advance in her signs but the bruit seemingly became less loud. The blood pressure remained the same. Her paranoid trend and the hallucinations of voices became progressively evident, and she was placed in an institution.

The combination of focal convulsive seizures and marked increase in the vascular markings of the skull should have suggested the possibility of a cerebral arteriovenous aneurysm. Had a bruit been listened for over the head the diagnosis could have been made before operation. Even so, an exploratory operation would have been justified because meningiomas, which these lesions are likely to resemble in their clinical manifestations, sometimes possess a bruit and comparable vascularity of the skull. The decompression and the roentgenotherapy, one or both, seem to have afforded some benefit, for the convulsive attacks have been much less severe and less frequent. The possible causative relation of the cerebral lesion to the psychosis is purely speculative. The several psychiatrists who examined the patient were about equally divided on the question.

Case 3. Recurring convulsions since the age of 14 in a boy 20 years old. Cephalic bruit. Distortion of ventricles seen by ventriculography. Arteriovenous aneurysm of right frontoparietal area of brain disclosed by osteoplastic exploration. Subtemporal decompression. Maximum roentgenotherapy. Ligation of right common and external carotid arteries. Cerebral angiography. Ligation of left internal and external carotid arteries. Marked diminution in cephalic bruit and cessation of grand mal convulsions one year after last operation.

First admission to the hospital October 6, 1936. Mike B., aged 20 years, an electrician's helper, complained of recurring convulsive seizures which had been present since the age of 14.

The patient's birth had been unremarkable and he had had no notable illnesses or injuries. At the age of 14 he began to have convulsions which recurred about every 3 months at first, but gradually increased in frequency until they averaged one a week. About one-fourth of the attacks occurred at night. The attacks were all generalized and associated with loss of consciousness but sometimes there were short prodromal symptoms in the left arm. Regular doses of phenobarbital failed to diminish the attacks.

Examination revealed his general physical condition not remarkable and his intelligence average. Prominent, pulsating vessels were present over the right frontotemporal area and in the midforehead. The blood pressure averaged 110/66 on each side, the cardiac rate was 75, and there was a faint systolic murmur at the apex. A bruit synchronous with the pulse was audible, over the right frontal and parietal regions of the head and over both eyeballs. There was no increased pulsation of the vessels of the neck but there was a bruit over those on the right. Compression of the right carotid artery diminished the bruit; compression of the left caused no change. The bruit was not audible to the patient. The optic

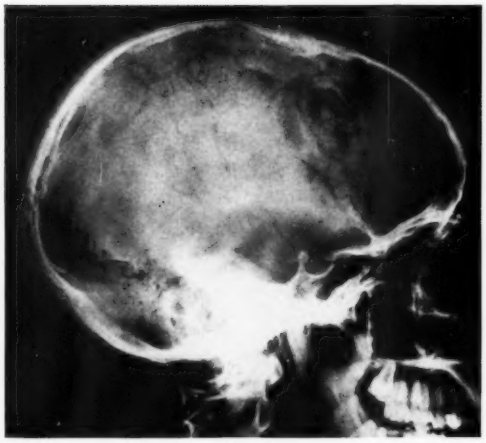


Fig. 4a. Case 3. Lateral roentgenogram of the skull showing rarefied areas in the right frontoparietal region resulting from direct pressure of the vessels of the aneurysm.

Fig. 4b. Case 3. Roentgenogram of the base of the skull showing enlargement of the right foramen spinosum.

fundi were normal in appearance. The motility functions, sensation, and reflexes were normal.

Blood and urine tests were normal. The spinal fluid was under slight increase in pressure (200 mm. of water). Roentgenographic studies of the heart and the electrocardiogram were normal.

Roentgenograms of the head (Figs. 4a and b) showed the cranium to be of normal size, shape, and thickness. The frontal sinuses were large and equal. There was very slight accentuation of the convolutional markings of the skull and slight thinning of the posterior clinoids but no frank evidence of increased intracranial pressure. There were several areas of rarefaction of the inner table of the right parietal bone, the result of erosion from large, pulsating vessels of the aneurysm. The vascular markings (diploe) were moderately accentuated on both sides. The grooves for the middle meningeal arteries were accentuated on both sides but more so on the right and the foramen spinosum on the right was twice the size of that on the left. There were no intracranial calcifications.

Pneumoencephalography was carried out October 7, 1936. One hundred and twenty cubic centimeters of fluid were removed and an equal amount of air was injected without producing any noteworthy change in the patient's condition. Roentgenograms showed the ventricles to be of normal size, but the body and frontal horn of the right lateral ventricle were depressed and the entire ventricular system was displaced slightly to the left. The markings of sulci over right hemisphere were distorted.

A diagnosis of arteriovenous aneurysm of the right parietal region was made.

Operation was performed October 10, 1936. After ether anesthesia had been administered, a right parietal osteoplastic flap was made. The vascularity of the scalp was somewhat increased and the bone bled freely from the cancellous portion; one diploetic vein actually spurted blood. The dura was not adherent to the bone but the middle meningeal artery was large and thicker walled than usual and the groove it had caused in the skull was deep. Several rounded bluish humps of the dural surface gave clues to the presence of large cortical vessels beneath. Rounded erosions in the skull were the imprints from the pressure of these vessels. The dura was reflected from the brain revealing a mass of tortuous, sometimes intertwining and overlapping vessels, some of which measured a centimeter or more in diameter. They partly overlay the motor cortex but were chiefly anterior to it and appeared to continue on beyond the exposure, anteriorly and superiorly. The vessels all had a reddish color; some were thin walled and arterial blood was seen streaming through them with each pulsation. A faint thrill was detected upon palpation of the vessels. In a number of places the dura was adherent to the pia-arachnoid by either flimsy or tough fibrous bands and at other places short vessels, 1 to 2 millimeters in diameter, passed directly from the cortical vessels to the dura. No attempt was made to ligate any of the cortical vessels but the dura was freed all around and the vascular attachments were transected. A fair sized subtemporal decompression was created before the flap was replaced and sutured.

Recovery from the operation was prompt and uneventful but for a convulsion 10 days after operation which, for the first time, was followed by a left hemiparesis that did not clear up for several days. Roentgenotherapy directed to right parietal region of the head was started before he left the hospital.

For the next 28 months he came regularly for roentgenotherapy and received 600 r units to each

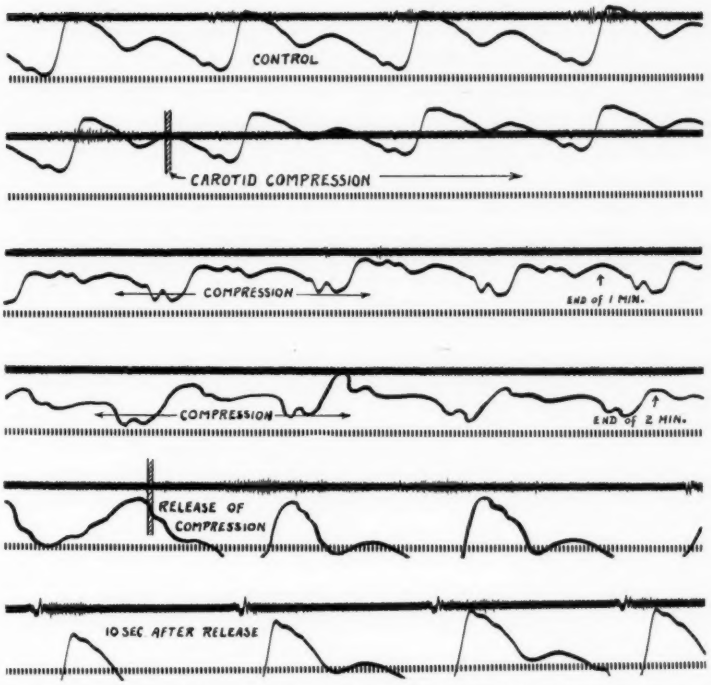


Fig. 5. Case 3. Stethographic record of cephalic bruit and simultaneous pulse record showing marked diminution in bruit with compression of the left common carotid artery.

of two parietal ports with each series. The series was repeated about every 8 weeks until he had received a total dosage of 13,200 r units. This resulted in complete and permanent alopecia of the scalp in the right parietotemporal region and comprised the limit of possibilities with irradiation. Although the major attacks were less frequent during this period after operation, petit mal seizures occurred on an average of every week; the latter were characterized by turning the head to the left and strongly flexing the left upper extremity. The decompression sometimes appeared full but never tense except just after a major convulsion.

Second admission to the hospital March 15, 1939. Because of the lack of material change in the number of convulsive seizures, although the proportion of major seizures had lessened, and because the maximum of roentgenotherapy had been given, he was readmitted for further operative procedure.

Although the irradiation had caused alopecia, some atrophic changes and telangiectasis of the scalp, there were in the region several tortuous and pulsating superficial vessels which obviously had not become thrombosed as a result of the therapy. The decompression was flat. The bruit was the same as it had been originally but its intensity was greatly diminished by compression of the right common carotid artery. A stethographic record of the bruit with and without compression of the carotid showed this diminution. Since repeated and prolonged compression of the carotid produced no untoward effects, ligation of the vessels in the neck was decided upon.

Operation was done March 23, 1939. Occlusion of the right common carotid artery was accomplished by ligation with autogenous fascia lata and of the right external carotid artery by wrapping it with double silk. The arteries were estimated to be about twice normal size when first exposed, and there was a palpable thrill over them.

Postoperative and subsequent course. Recovery from operation was uncomplicated, and no signs of palsy developed. There was no material change in the blood pressure or pulse. The bruit over the head became faint and was indistinct over the right eyeball; over the left globe it remained the same. For the next 7 months the intensity of the cranial bruit increased somewhat but was less than its original intensity. The convulsions changed neither in quality nor frequency and after a series of 6 successive major attacks he was readmitted to the hospital. The use of sodium diphenyl hydantoinate for 3 months did not alter the convulsive seizures.

Third admission to the hospital was November 13, 1939. Because of continuation of convulsions without material improvement after subtemporal decompression, maximum roentgenotherapy, and occlusion of the right common and external carotid arteries, he was admitted for restudy and, possibly, further operation.

Examination showed no essential changes from those recorded heretofore except that vessels of the scalp had become more prominent on the left side since the ligation of the right carotid arteries. There was no change in motility function, sensation, or reflexes. The decompression was slightly full but soft and pulsated freely. The bruit was readily heard over the decompressed area but faintly over the right frontal area and over the right eyeball; it was loudest over the left eyeball and of moderate intensity over the left carotid. The blood pressure remained at an average of 110/80 and the cardiac findings were normal.

Electroencephalography was carried out by Dr. D. J. Simon. A summary of the findings showed abnormal cortical function over both cerebral hemispheres. The abnormality appeared greatest in frontal areas and was approximately equal on the two sides.

Compression of the left common carotid artery caused the bruit to disappear completely during the first 10 seconds. Thereafter a soft, low pitched bruit appeared and remained so during 5 minutes of compression. Compression of the artery for this length of time caused no loss of consciousness or special symptoms other than a full feeling in the head which was probably due to the simultaneous compression of the left internal jugular vein.

A stethographic record (Fig. 5) of the cranial bruit was taken before, during, and after 2 minutes of continuous occlusion of the left common carotid artery. This record showed the disappearance of the major part of the bruit. It was interesting to find that with this sensitive machine, by which intensity and frequency of sound could be recorded, there was relatively greater change following occlusion of the carotid than one might have guessed by merely listening with an ordinary stethoscope.

It was postulated that since the patient was still young and no untoward reaction followed 5 minute occlusion of the remaining common carotid artery, ligation of the artery would be comparatively safe and possibly beneficial.

Cerebral angiography was carried out November 24, 1939, after the injection of 20 cubic centimeters of thorium dioxide solution into the left common carotid artery. With the use of local anesthesia the left common carotid artery was exposed through a short incision. Just below the bifurcation of the artery the material was rapidly injected and roentgenograms were taken 4, 10, and 16 seconds after the injection was started.

The first roentgenogram (Fig. 6) showed the material crossing the anterior communicating artery and outlining the vessels of the aneurysmal lesion on the right side. None of the cerebral vessels on the left side or elsewhere were visualized. On the second and third plates there was no evidence of the material remaining.

Immediately following the angiography, November 24, 1939, the patient was returned to the operating room and after local injection of procaine anesthesia the carotid arteries on the left were more widely exposed. The common and internal carotids were estimated to be about half again their normal size, and there was a faint thrill palpable over them. With traction and manipulation of the common carotid, the blood pressure suddenly rose to 200/120 and the pulse to 140 but they promptly returned to normal when the manipulations were discontinued. There was no recurrence of the phenomenon after injection of procaine into the carotid plexus at the bifurcation. A temporary ligature was placed upon the internal carotid and the patient was observed for 30 minutes. Since no untoward symptoms or signs developed, an occluding aluminum band was placed on the internal carotid artery just above the bifurcation.

Samples of blood were taken from the left internal jugular vein before and again 10 minutes after occlusion of the left internal carotid. The oxygen and carbon dioxide contents of the blood were as follows:[1] Before ligation of the artery—oxygen content, 19.8 volumes per cent; carbon dioxide content, 51.8 volumes per cent. After ligation of the artery (10 minutes after)—oxygen content, 14.8 volumes per cent; carbon dioxide content, 55.4 volumes per cent.

There were no postoperative complications. One short left sided convulsion, without loss of consciousness, occurred 12 hours after operation but there were no aphasia, palsy, or other untoward developments. The cephalic bruit was very greatly diminished in intensity and remained so. The bruit over the left eyeball, however, was markedly accentuated after the ligation, and the superficial vessels of the left side of the scalp became more prominent.

Operation again was performed December 7, 1939. After local procaine anesthesia, the 12 day old wound in the neck was reopened. A temporary ligature was placed upon the left external carotid artery and the patient observed for 20 minutes. Since no untoward symptoms or signs developed the artery was occluded by wrapping it with silk just above the bifurcation of the common carotid. The superior thyroid artery which was larger than normal was also occluded with a silk ligature.

Samples of blood were taken from the left internal jugular vein before and again 10 minutes after occlusion of the left external carotid and superior thyroid arteries. The oxygen and carbon dioxide contents of the blood were as follows: Before ligation of the arteries—oxygen content, 15.7 volumes per cent; carbon dioxide content, 54.8 volumes per cent. After

[1]The normal range for oxygen and carbon dioxide content of the blood is as follows: Arterial blood—oxygen content, 15 to 23 volumes per cent; carbon dioxide content, 45 to 55 volumes per cent. Venous blood—oxygen content, 10 to 18 volumes per cent; carbon dioxide content, 50 to 60 volumes per cent. The figures represent weighted averages of several investigators (11).

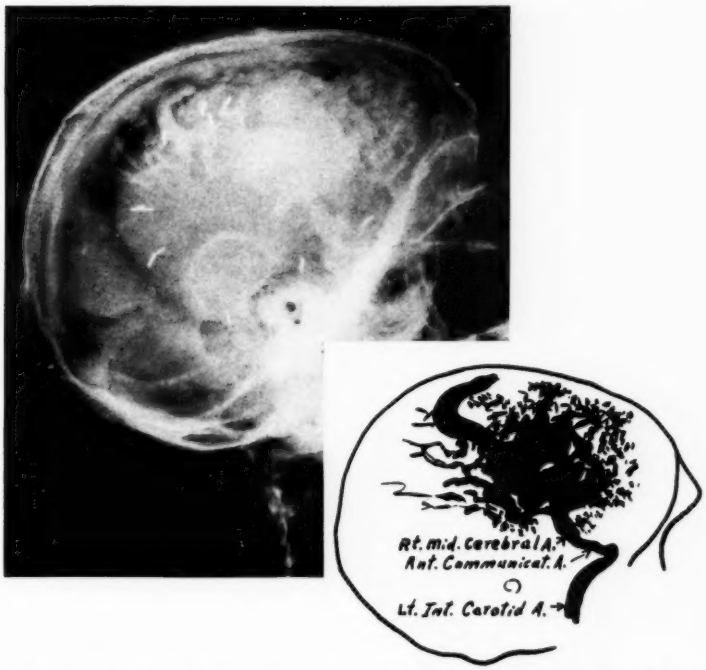


Fig. 6. Case 3. Cerebral angiography with injection of 20 cubic centimeters of thorotrast in the left common carotid artery. The substance has crossed to the right side and shows the large mid-cerebral artery feeding the "nest" of smaller vessels which connect with large veins near the sagittal sinus.

ligation of the arteries (10 minutes after)—oxygen content, 14.8 volumes per cent; carbon dioxide content, 57.1 volumes per cent.

Recovery from operation was uncomplicated. The intensity of the bruit over the left eyeball was materially diminished.

For several weeks after leaving the hospital he experienced momentary unsteadiness and blurring of vision on rising from a sitting or reclining position but this eventually ceased. In the year after operation he had no recurrence of grand mal convulsions. Attacks of uncontrolled, momentary turning of the head to the right without loss of consciousness occurred on an average of once a week. Paresthesias without convulsive movements or loss of power occurred in the left upper and lower extremities every 6 to 8 weeks. The bruit a year after operation was of low intensity over the left eyeball, almost undiscernible over the right eyeball, and very faint on the right temporoparietal region of the head. There were no visual or auditory disturbances, no palsies of the extremities, and no changes in sensation or in reflexes. He was taking .030 grams of phenobarbital three times daily, said he felt remarkably well, and was actively employed in a business of his own.

The close observation of this individual and the use of a succession of therapeutic measures over a period of 3 years have provided an abundance of information about cerebral arteriovenous aneurysms in general. It has been demonstrated that: The use of the maximum dosage of roentgenotherapy cannot be relied upon to affect the lesion, although it may well be that better results would have been obtained if the arterial ligations had been carried out first in order to diminish the blood flow through the lesion. Successive ligations of all the carotid arteries in both sides of the neck can be done, at least in some persons, with comparative safety. Doubtless youth and the extensive collateral circulation in the presence of the aneurysm makes this possible. There is extensive collateral circulation between the internal and external carotid systems, partly through the orbit. The effectiveness of diminishing the spill of arterial blood into the ve-

Fig. 7. Case 4. Photograph showing relative enlargement of the head.

nous system by ligation of a carotid artery can be estimated by determining the oxygen and carbon dioxide content of the blood of the jugular vein before and after the ligation. The arterial anastomosis through the anterior communicating artery of the circle of Willis and the increase in the circulation time in the brain can be safely demonstrated by the injection of thorium dioxide into the carotid artery. Convulsions can be materially benefited by extensive occlusion of the carotid arteries.

The acute rise in pulse rate and blood pressure that occurred on manipulation of the carotid is an interesting phenomenon but has no special relation to the subject under discussion. It resulted, probably, from sudden decrease in the intrasinal pressure on occlusion of the common carotid artery. Similar experiences have been mentioned by others (8, 23).

CASE 4. Two episodes of transient hemiparesis in a child of 2½ years. Large head, prominent vessels of the scalp and cephalic bruit. Right cerebral arteriovenous aneurysm demonstrated by angiography and pneumoencephalography. Successive ligation of carotid arteries. Death following last ligation. Autopsy.

On December 13, 1938, George S., aged 2½, referred by Dr. Edgar Mayer of New York City, was admitted to the hospital with the complaint of attacks of transient left hemiparesis.

The child's birth was not remarkable and he was thought to be a bright and healthy boy until 2

Fig. 8. Case 4. Infrared photographs showing increased vascularity of the scalp.

months before admission when he stumbled on a stairs and fell bumping his head. Not much was thought of this incident until 12 days later when it was noticed that his left foot was so weak he could hardly walk and within a short time thereafter the left arm hung limply. Over night he regained complete use of these extremities. A second and similar episode occurred 6 weeks later (1 week prior to admission).

On examination, the child was found to be happy, co-operative and, by Binet psychometric tests, to have "average intelligence and a fairly even level of function." The head appeared and measured larger in all dimensions than normal (Fig. 7). Veins of the scalp were unusually prominent and some pulsated (Fig. 8). On auscultation a bruit could be heard all over the head and over both eyeballs. Both a bruit and a thrill were present over large, briskly pulsating vessels in the neck. The retinal vessels were full and tortuous, particularly on the right, and the right pupil was larger. There was no exophthalmos or pulsation of the eyeballs. There was slight but definite left hemiparesis and increased deep reflexes on that side. The heart was enlarged and there was a systolic murmur heard all over the precordium. The blood pressure averaged 104/70 on both sides; the cardiac rate was 70 and the character of the pulses was suggestive of a "Corrigan pulse." Compression of either carotid in the neck diminished the intensity of the bruit, but compression of the right carotid produced the greater effect.

Laboratory tests on the blood and urine showed no abnormality. Spinal fluid examination showed questionable, slight increase in pressure but no other unusual findings; the total protein was .030 grams per cent and the cell count was normal. Electrocardiogram showed a slight left ventricular preponderance. Roentgenograms of the chest (Fig. 9a) showed moderate enlargement of the heart to the right and to the left, also moderate widening of the superior vena cava.

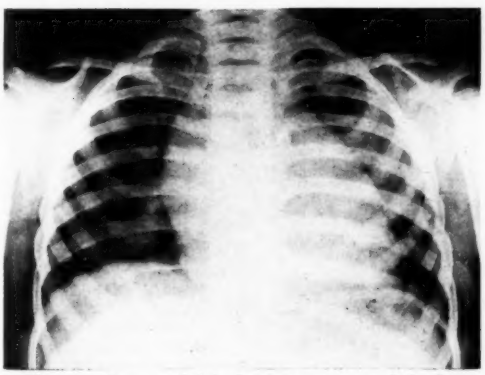


Fig. 9a. Case 4. Original roentgenogram of the heart showing general enlargement, more particularly to the right.

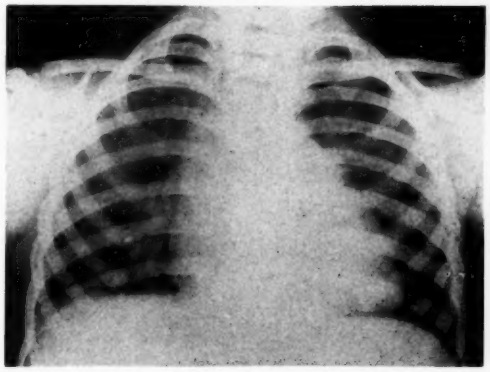


Fig. 9b. Case 4. Roentgenogram of the heart 4 weeks following ligation of the common and external carotid arteries on the side of the lesion. Note the diminution in the size of the heart as compared to the roentgenogram taken before operation (see Fig. 9a).

Roentgenograms of the head showed a thin skull and enlargement of the cranial vault. However, there was no widening of the sutures, or other signs suggesting increased intracranial pressure. The vascular markings of the skull (diploe) were slightly accentuated in frontal regions, more on the right. The groove for the right middle meningeal artery was larger than the left; no change in size of either foramen spinosum. There were no local areas of erosion in skull and no intracranial calcification.

Pneumoencephalography was done January 25, 1939. Ninety cubic centimeters of air were injected without producing any change in the patient's condition. Roentgenograms showed the left lateral ventricle to be larger than the right and the right one appeared slightly depressed; both were shifted slightly to the left. The sulcal markings over the right cortex had a curious mottled appearance.

Cerebral angiography was carried out, January 25, 1939, after the injection of 15 cubic centimeters of thorium dioxide solution into the right common carotid artery. After the administration of ether anesthesia the right common carotid artery was exposed through a short incision just below its bifurcation. Under vision, thorium dioxide was rapidly injected in 3 seconds and roentgenograms were taken immediately, while compression was kept on the proximal portion of the artery to diminish the flow of blood. A second plate was taken 7 seconds after the first and a third plate in another 7 seconds.

The first roentgenogram (Fig. 10) showed good filling of the right cerebral vessels and in the parietal region demonstrated many tortuous abnormal channels characteristic of an arteriovenous aneurysm. The second plate still showed faint shadows of the dispersed material but the third plate showed none.

Roentgenogram of the abdomen 5 days later showed the liver and spleen to cast dense shadows from the deposited thorium salt.

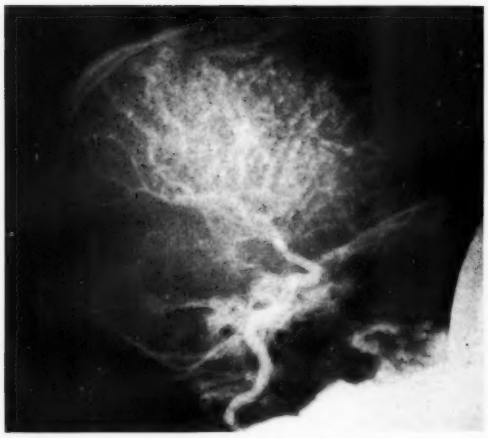


Fig. 10. Case 4. Cerebral angiography by injection of 15 cubic centimeters of thorotrast in the right common carotid artery. Note the short course of the mid-cerebral artery before it empties into the "nest" of smaller vessels which connect it with the larger veins near the sagittal sinus. The rolandic vein can be seen to be enlarged all along its course.

Fig. 11. Case 4. Cerebral angiography by injection of 35 per cent diodrast in the left common carotid artery. Note the outline of normal vessels on the left side of the brain and the partial outline of abnormal vessels of the right frontal lobe. The dye has crossed through the anterior communicating artery. Note that a more anterior portion of the vascular lesion is outlined than in Figure 10.

Operation was performed February 15, 1939. After ether anesthesia had been administered, occlusion of the right common carotid artery was accomplished with a ligature of autogenous fascia lata and of the right external carotid artery with a ligature of double silk. These arteries were larger than would be expected in a normal child of this age. The internal jugular vein also was large and pulsated.

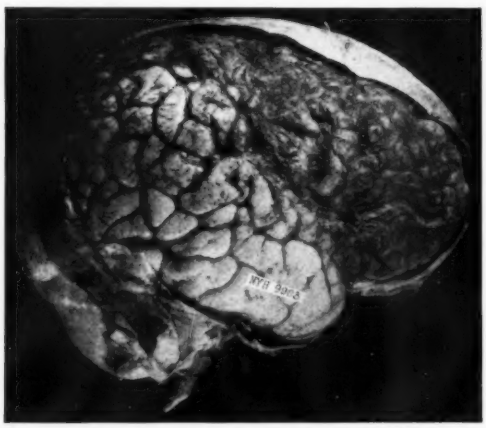


Fig. 12. Case 4. Photograph of right side of the brain showing extensive distribution of the vascular lesion over the entire right frontal lobe as far back as the rolandic fissure.

Fig. 13. Case 4. Coronal section of the brain passing through the tips of the temporal lobes. The entire right hemisphere has a shrunken appearance which is the result both of the collapse of the numerous blood vessels and of the atrophy of the parenchyma. Many abnormal vessels are apparent on the surface, in the sulci, and in the substance of the hemisphere.

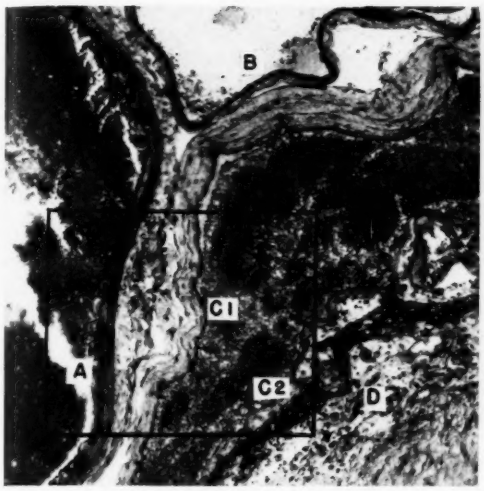


Fig. 14a. Case 4. A section through the cerebral cortex shows the walls of three adjacent vessels. One is a relatively thin walled artery *A*, and the 2 others are veins. One vein has an unusually thin wall, *B*, while the other has a thin wall on one side, C_1, and a greatly fibrosed and thickened wall on the other, C_2. There is phagocytic infiltration and softening of the brain, *D*, adjacent to the vein. (Masson stain, ×45.)

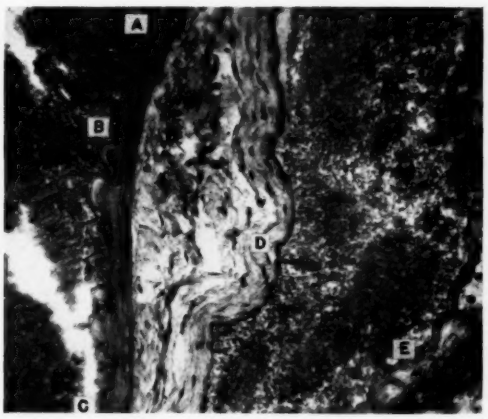


Fig. 14b. Case 4. Enlargement of area outlined in Fig. 14a. There is a region in the circumference of the artery (*A* to *B*) which is without elastica interna; elsewhere (*B* to *C*) there is a well developed elastica interna. Segments of the opposed walls of a single vein show the great fibrosis and thickening of one side (*D*), and the relatively thin wall of the other side (*E*). (Masson stain, ×68.)

There was no immediate untoward reaction as a result of the operation. The intensity of the bruit over the head was only slightly diminished although that heard over the right eyeball was now about one-fourth that over the left. There was no material change in the blood pressure or pulse but a roentgenogram of the heart (Fig. 9b) 4 weeks after the ligation showed a distinct diminution in the cardiac shadow, principally on the right side. On the second day after the ligation there suddenly developed marked weakness of the left side of the body. Since it came so long after the arterial occlusion, its occurrence was considered fortuitous and there was thought to be no reason for removing the ligatures. The weakness gradually disappeared over the next 10 days but suddenly recurred at the end of this period. This time a lumbar puncture was performed with the idea of demonstrating bloody spinal fluid, since these recurring palsies were thought to be due to successive hemorrhages; but the fluid contained no blood, no increase in white cells, or change in its protein content.

During the first 12 months after operation there were two additional episodes of transient left hemiplegia; like the others they came on rather rapidly over a period of several minutes during which time the child did not complain, had no convulsive movements, and did not lose consciousness. Recovery from each succeeding attack was less complete so that there developed considerable restriction in motion of the left extremities and he walked with a spastic gait. The vascularity of the scalp did not diminish from its original state nor did the bruit over the head change, although it was much less distinct over the right eyeball.

In February and March, 1940, over a year after operation, there were several attacks of transitory left hemiplegia and he complained frequently of severe pain in the frontal and temporal regions of the head, worse on the right side. Compression for 5 minutes of the left carotid artery at the bifurcation

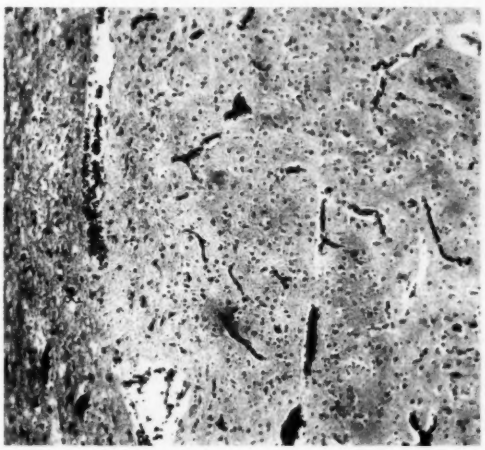


Fig. 14c. Case 4. A section through the cerebral cortex shows the marked increase in number and size of the small vessels of the gray matter. (Pal-Weigert stain, ×35.)

diminished the intensity of bruit over the head 75 per cent and did not cause any untoward signs or symptoms.

Second admission to the hospital was on April 23, 1940. Because of the increasing symptoms and the apparent safety of occlusion of the carotid arteries on the left side of the neck the child was brought back to the hospital for the purpose of ligation of these arteries.

Examination showed no essential changes from those recorded heretofore. The Rorschach psychometric test gave no indication of organic disease of the brain. Development was normal for his age except that the head was still disproportionately large and the left hemiplegia was more marked; the lower extremity was more palsied than the upper. There were no demonstrable changes in vision or in sensation. The bruit was distinct over the right side of the head, left eyeball, and left carotid in the neck, faint over the left side of the head and absent over the right eyeball. The blood pressure was 106/70 and the cardiac rate 70. The heart on roentgenogram was seen to have regained its original size and shape. The electrocardiogram was unchanged.

In preparation for operation the left carotids over the bifurcation were repeatedly compressed for 4 to 5 minute intervals for 4 days.

Cerebral angiography was carried out April 27, 1940, after the injection of 25 cubic centimeters of 35 per cent diodrast into the left common carotid artery. After ether inhalation anesthesia had been administered the left common carotid artery was exposed just below its bifurcation. The diodrast was rapidly injected in about 4 seconds and 3 roentgenograms were taken, one at the termination of the injection and 2 others at 7 second intervals.

The first roentgenogram (Fig. 11) showed the outline of some of the cerebral arteries on the left which appeared normal and the anomalous vessels of the right hemisphere which had been demonstrated previously after injection of thorotrast into the right carotid artery. No dye was visible on the second and third roentgenograms. No noteworthy incidents developed during or after the angiography and, since the child's condition appeared satisfactory on his regaining consciousness, he was returned to the operating room for ligation of the carotid arteries.

Operation was performed April 27, 1940. After resumption of ether inhalation anesthesia the left carotid arteries at the region of the bifurcation were exposed. These arteries were definitely larger than normal. After trial occlusion of the internal carotid for 20 minutes no unusual signs developed and the vessel was ligated with several strands of silk. The external carotid was ligated in similar fashion.

Samples of blood were taken from the left internal jugular vein before and again 10 minutes after occlusion of the left carotid arteries. The oxygen and carbon dioxide contents of the blood were as follows (see Case 3 for normal values): Before ligation of the arteries—oxygen content, 20.2 volumes per cent; carbon dioxide content, 48.8 volumes per cent. After ligation of the arteries (10 minutes after)—oxygen content, 14.0 volumes per cent; carbon dioxide content, 55.6 volumes per cent.

There had been no noteworthy changes in the child's general condition during the operation and at its termination the pulse rate was 130, blood pressure 130/60, and respiration normal. The bruit could not be heard over the head but was of medium intensity over the eyeballs. Recovery from anesthesia was slow but no alarming signs developed until 4 hours after operation when twitching movements began in the left side of the body. Complete consciousness was not regained but there was restless movement of the head and right extremities and response to painful stimuli. The left sided convulsive movements occurred at first about every 5 minutes and lasted 10 to 30 seconds but gradually they increased in frequency and became almost constant. Occasionally there were convulsive twitchings of the right side as well.

On April 27, 1940, 6 hours after the carotids had been ligated the child was returned to the operating room for removal of the ligatures. The wound in the left side of the neck was reopened and the occluding ligatures on the carotid arteries were removed. There had been no injury to the vessel walls and there was no evidence of thrombosis for the arteries promptly filled with blood and pulsated briskly. There was also prompt improvement in the quality of the pulse and respiration, relaxation of the extremities, and subsidence of convulsive twitchings.

Although there was temporary improvement after removal of the ligatures occluding the carotids, within several hours the convulsive twitchings became more frequent and involved all extremities. There was marked rigidity of the extremities, pulse rate rose to 200 per minute, blood pressure was unobtainable, and temperature rose to 41 degrees C. The condition remained critical and various supportive measures were ineffectual. Death occurred 3 days after operation, April 30, 1940.

Postmortem examination was limited to the brain and the thorax. A section of liver was also removed for study. Before the skull was opened the left internal carotid artery and internal jugular vein were cannulated and the vessels of the brain were suffused first with saline solution and then with 10 per cent formalin. After the brain had fixed *in situ* it was removed together with the dura. The foramen spinosum on the right measured 3 millimeters and on the left 1.5 millimeters in diameter. The right internal carotid artery at the foramen lacerum measured 3 millimeters in diameter and the left 5 millimeters.

The surface of the entire right frontal lobe was covered with many thin walled vessels of various sizes (Fig. 12). There were numerous short vessels of 1 to 2 millimeters in diameter connecting these cortical vessels to the dura and presumably to the dural arteries. The gyri of the right cerebral hemisphere particularly in the frontal lobe were smaller than those on the left and the entire right hemisphere was smaller than the left. Fluid injected into the

right internal carotid artery at the circle of Willis quickly distended some of the larger vessels on the lateral surface of the right frontal lobe but more complete injection of all the vessels was prevented because of tears in the walls of some. Fluid injected into the left internal carotid was seen to pass readily across the relatively large anterior communicating artery and into the vessels over the right frontal lobe.

Coronal section just behind the tip of the temporal lobes showed the small size of the right hemisphere as compared to the normal appearing left hemisphere (Fig. 13). The entire aspect of the cut surface of the right side was dark and many abnormal vessels were seen throughout the gray and white matter as well as in the corpus callosum on that side.

The brain nowhere showed any thrombosis of the vessels or evidence of recent hemorrhage.

The heart weighed 160 grams. The right ventricular wall measured 2 millimeters in thickness and the left 10 millimeters. Apart from slight dilatation and hypertrophy, the heart was usual in appearance.

Microscopic examination (Figs. 14a, b, c) revealed the following: Sections through the cortex of the right frontal lobe showed many superficial veins and a few arteries, all of large caliber, thin walled, and irregularly shaped. In the substance of the brain, particularly in the white matter, were numerous, often closely placed, large and small blood channels, the majority of which resembled veins. The thickness of the walls of these vessels varied greatly and was not uniformly in proportion to the size of the lumen. In some veins with relatively thicker walls the thickening of the media suggested faulty attempts at arterial structure. Elastic tissue stains showed a comparatively few of the vessels possessing definite elastica interna but in many there were delicate elastic fibrils scattered throughout the walls. The capillaries of the gray matter in particular, were greatly distended with blood. The vessels were mostly separated by interstitial tissue in which varying quantities but no notable increase of glial fibers existed. In places there were distinct areas of necrosis containing phagocytes and many small blood vessels in the interstitial tissue particularly in the cortical gray matter. Nowhere was there thrombosis or calcium deposit.

The tissue of the liver was of normal appearance except that, in many places in the periphery of the lobules and around the central veins, were small, unevenly deposited masses of brown granular material. This material, the deposited thorium compound, appeared to be inert and was unattended by any significant changes in the adjacent tissue.

While the child's first recognized episode of transient hemiparesis followed a few weeks after a fall and a bump on the head, there is no justification for ascribing the cerebral arteriovenous aneurysm to trauma. There is every indication that the lesion is a congenital one, though it is interesting to speculate on why

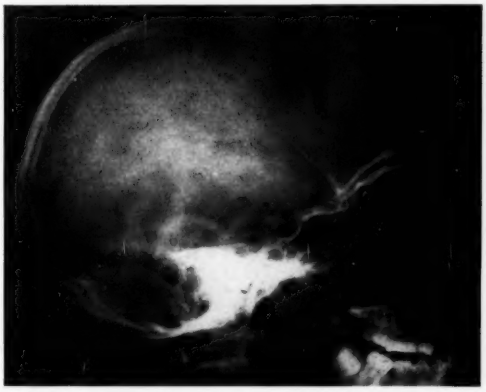


Fig. 15. Case 5. Lateral view of the skull showing in particular the local areas of rarefaction in the parietotemporal region resulting from direct pressure of the vessels of the aneurysm. Note fine calcified shadows in central region.

there were no neurological signs before the age of 2½ and indeed how and why attacks of hemiparesis occurred at all. Since these aneurysmal formations have a reputation for bleeding, the first thought was that the attacks resulted from recurring hemorrhage. It may be that small subpial hemorrhages were responsible but there were none of the clinical signs of subarachnoid hemorrhage at any time and the cerebrospinal fluid was found to be clear a short time after one of the attacks. Thrombosis of some of the vessels is also a possible explanation of the attacks for it has been known to occur spontaneously in such lesions and in fact is the principle upon which roentgenotherapy is based in the hope of obliterating the lesion. However, in the sections examined after death no thrombosed or obliterated vessels were encountered.

The injection of thorium dioxide on one occasion and diodrast on another served not only to verify the diagnosis but also to give some idea of the location, size, and extent of the vessels of the aneurysm. The thorium observed in the sections of the liver appeared after 15 months to be inert and to have caused no demonstrable local effects in the tissue. Diodrast gave an outline of the intracranial vessels equal to that produced by the thorotrast, and there is no indication on clinical or pathological findings that the injection of diodrast was a contributing factor in the child's death.

Fig. 16. Case 6. Lateral view of the skull showing local area of rarefaction in the parietal bone due to pressure from a large vessel of the aneurysm (see also Fig. 17).

Fig. 17. Case 6. Retouched photograph taken at the operating table. Arrow points to the vessel which caused thinning of the dura and erosion of the skull seen in Figure 16. Inset indicates the site of the operative exposure.

It is assumed that the principal value of occlusion of the carotid arteries lies in the diminution of the total arterial supply to the aneurysm, thus easing the strain upon the thin walled veins and lessening the possibility of their rupture. It proved after the first operation in this case to have the additional value of taking sufficient load off the heart to diminish its size.

Since the successive occlusion of the carotid arteries in Case 3 had been uncomplicated no difficulties were anticipated in this case. Cerebral anoxia which undoubtedly caused death might have been avoided had but one artery, either the internal or the external (or the common) carotid on the left, been occluded at a time instead of both of the former.

Case 5. Weakness, unsteadiness, underdevelopment of right extremities since infancy and daily headaches for one year in girl, 14 years old. Cephalic bruit, prominent vessels of the scalp and right hemiparesis found on examination. Calcified areas in left cerebrum. Distortion of ventricles and of sulcal markings seen by pneumo-encephalography. Ligation of left common and external carotid arteries. Diminution in bruit and improvement of headaches 1½ years later. On April 10, 1939, Marie L., a 14 year old school girl, referred by Out Patient Department, was admitted to hospital complaining of headache, weakness, and tremor of right extremities.

The girl's birth was uncomplicated but since infancy it was noticed that the right upper and lower extremities were weak, clumsy, and tremorous; she learned to use her left hand although it was supposed that she was naturally right handed. She had never had a convulsion.

A year before admission she developed recurring, severe, left frontotemporal headaches. They came almost daily, usually appearing the first thing in the morning, and lasting 2 to 3 hours. They were dull, throbbing, and occasionally associated with nausea.

Examination disclosed a quiet, intelligent girl who walked clumsily with the right leg and held the right arm close to the side. Speech was normal. The head was thought to be slightly larger than normal but not enough so as to distort her appearance. The vessels of the scalp in the left frontotemporal region were prominent and pulsating. There was no prominence or pulsation of the eyeballs. A bruit of low intensity was heard over the left frontotemporal region, less distinctly over the right side of the head, but equally over both eyeballs. The patient was unaware of any noise in the head. The vessels of the neck pulsated excessively. A faint thrill was felt on light palpation over them and a bruit was heard on auscultation; these signs were greater on the left. The left pupil was slightly larger than the right but there was some variation in this finding. The vessels of the left retina were full and tortuous in comparison to those on the opposite side but otherwise the optic fundi were unremarkable. Visual acuity and perimetry were normal. The right extremities were both slightly underdeveloped in musculature and weaker in strength but of normal lengths. There was a gross ataxic intention tremor of these extremities and sometimes slow, vermicular, adventitious move-

ments of the hand. There were slightly increased resistance to passive stretch, exaggerated deep reflexes, and an extensor plantar response on the right side. The blood pressure averaged 100/50 in each arm. The pulse had a full bounding quality and a rate of 90. The cardiac findings were normal.

Blood and urine tests were normal. Roentgenograms of the chest showed nothing abnormal in the lungs, heart, or great vessels. The spinal fluid was under normal pressure and the laboratory findings on the fluid were within normal limits; the total protein content was .040 grams per cent.

Roentgenograms of the head showed slight enlargement of the cranial vault. The skull was thin, and the frontal sinuses were large, the left greater than the right. There were no signs of increased intracranial pressure. The vascular markings of the skull (diploe) were moderately accentuated on both sides, particularly in the frontal regions. The grooves for the middle meningeal arteries were accentuated and more so on the left than on the right. The foramen spinosum was not well visualized on either side. There were several areas of rarefaction in the left parietotemporal region, imprints of large vessels of the aneurysm (Fig. 15). There were numerous small calcified areas in the subcortical region of the left parietal lobe.

Pneumoencephalography was performed April 25, 1939. Seventy-five cubic centimeters of air were injected after an equal amount of fluid had been removed. Roentgenograms showed the air in the subarachnoid spaces over the left cerebral hemisphere to have a curious, mottled appearance unlike the shadows marking the normal sulci on the opposite side. The ventricles were not shifted but the left lateral ventricle filled poorly and had irregular, distorted outlines.

Cerebral angiography was done on April 27, 1939 after the injection of 15 cubic centimeters of thorium dioxide solution into the left common carotid artery. Rapid injection was done in the usual way and roentgenograms were taken in 4 seconds, 12 seconds, and 18 seconds, after the injection, but only in the first plate were scattered flecks of the material seen in left parietal region.

Operation was performed April 29, 1939. With the use of local infiltration of procaine, occlusion of the left common carotid artery was accomplished by ligation with a strip of autogenous fascia lata, and the left external carotid artery was occluded with a double silk ligature. These arteries were estimated to be half again their normal size.

Samples of blood were taken from the left internal jugular vein before and 10 minutes after the arterial ligations. The oxygen and carbon dioxide contents of the blood were as follows (see Case 3 for normal values): Before ligation of the arteries—oxygen content, 15.5 volumes per cent; carbon dioxide content, 48.7 volumes per cent. After ligation of the arteries (10 minutes after)—oxygen content, 12.8 volumes per cent; carbon dioxide content, 50.1 volumes per cent.

There were no untoward reactions following operation, no change in power or sensation on the right side of the body, no visual perimetric defects and no difficulty in speech. There was no change in the blood pressure or pulse. The bruit heard over the head was estimated to possess about one-half its former intensity. The bruit over the left eyeball was hardly audible while over the right eyeball the intensity was as great if not greater than originally.

During the first 3 months after leaving the hospital she had three convulsive seizures, each characterized by the successive appearance of inability to speak, paresthesias on the right side of the body, inability to move the right extremities, inability to see to the right, loss of consciousness for 5 to 10 minutes (without known convulsive movements) and headache on the left side of the head upon recovery. Phenobarbital in 15 milligram doses three times a day was prescribed after the second attack but later discontinued. No further convulsions occurred during the 18 months after operation.

The bruit over the head remained faint and was barely perceptible over the left eyeball, yet over the right eyeball it was loud. Compression of the right common carotid artery caused the bruit everywhere to become barely audible and after 4 minutes of compression there were no signs of cerebral anemia.

The headaches were markedly improved following ligation of the carotids and, since this was the complaint for which she requested relief, she was well satisfied. There were occasional headaches, less severe than her former ones, and on one occasion the injection of half an ampul (.25 mgm.) of ergotamine tartrate caused the pain to disappear promptly.

It is interesting that this child had sufficient damage to the left cerebral hemisphere to cause hemiparesis since infancy, yet had had no convulsive seizures until after the ligation of the carotid arteries. The ligation resulted in definite and sustained diminution in the intensity of the bruit and possibly thrombosis occurring in some of the smaller vessels of the aneurysm was the cause of the convulsions. Although the carbon dioxide and oxygen contents of the jugular blood returned to normal after ligation of the arteries, doubtless had additional samples been taken later, the improvement would be less marked since there was evidence of the persistence of the aneurysm. Still another noteworthy finding here was that no cerebral vessels were visualized by angiography though the test was performed as it always has been when satisfactory visualization of the vessels has resulted. The circulation time through the left hemisphere in this case may have been so rapid, due to direct

dumping of arterial blood into large venous channels, that the material injected was too rapidly diffused to cast a shadow.

CASE 6. Left sided convulsions for 6 years in man 42 years old. Cephalic bruit, not discovered before operation. Distortion of the ventricles seen by ventriculography. Arteriovenous aneurysm of right frontoparietal area of brain disclosed by osteoplastic exploration. Subtemporal decompression. Improvement in convulsions one year later.

On October 25, 1939, Edward R., aged 42, a clerk, referred by the Out Patient Department was admitted to the hospital, complaining of convulsive seizures for 6 years.

At the age of 36 he had his first convulsive seizure. It started in the left side of the neck with a tight feeling which spread to the face and arm on the same side. It was followed in a few minutes by loss of consciousness and a generalized convulsion involving mostly the left side of the body. Fourteen others occurred in the next 6 years and all followed the same pattern except that sometimes the onset was in the face or roof of the mouth on the left. All attacks were diurnal. The attacks lasted 15 to 20 minutes and were followed by drowsiness. He never had headache or any other significant symptoms.

Examination revealed nothing remarkable in his general physical condition and his mental attributes were above average. There were no nevi or abnormal pigmentations over the body. Blood pressure averaged 122/80 in each arm and the cardiac rate was 80. The heart findings were normal and the pulse was of normal quality. There was a faint bruit over the right frontoparietal area of the head, over both eyeballs, and over the right carotid artery (not discovered until after operation). The patient was unaware of the bruit. The carotid arteries in the neck were not unusual on palpation. There was no enlargement or pulsation of the vessels of the scalp and the retinal vessels were not remarkable. Other functions of the head were normal as were motility and sensory functions over the body. Reflexes were normal except for slight increase of those in the left upper extremity.

Blood and urine tests were normal. Electrocardiogram showed moderate left axis deviation indicative of hypertrophy of the left side of the heart but a roentgenogram of the heart showed only slight enlargement to the left.

Roentgenogram of the skull (Fig. 16) showed a normal vault but some thinning of the bone of the right parietal region. The frontal sinuses were large, the right larger than the left. There were no signs of increased intracranial pressure but there were oval shaped areas of rarefaction in the right parietotemporal area due to pressure of the large vessels of the aneurysm. Also the vascular markings of the cranium (diploe) were accentuated, and the groove for the right middle meningeal artery was deeper and wider than usual.

Lumbar puncture (in horizontal position) showed an initial spinal fluid pressure of 150 millimeters of water and normal rise and fall of the pressure on jugular compression. The examination of the fluid showed a total protein of .040 grams per cent.

The electroencephalogram showed pathological waves in all frontal leads without lateralizing signs.

Ventriculography was carried out November 15, 1939. Twenty cubic centimeters of clear fluid were exchanged for air. Roentgenograms showed irregular filling of the body of the right lateral ventricle and slight depression of the right frontal horn, also, slight shift of both lateral ventricles and the third ventricle to the left.

The supposition was that the lesion was possibly a small right parietal meningioma.

Operation was performed November 15, 1939. After ether anesthesia had been administered, a right parietal osteoplastic operation was performed. Neither the scalp nor the bone was found to be unusually vascular and the dura was not adherent to bone. However, the middle meningeal artery was tortuous and twice the usual size. At one place the dura was humped up, thinned out, and bluish in color because of a large, pulsating cortical vessel beneath. It was this vessel that had caused the prominent area of erosion in the bone and the depth of the depression in the bone was about 5 millimeters. Elsewhere the dura had a wavy appearance as it was humped up by other large vessels beneath it and there were shallower depressions in the bone corresponding to some of these vessels. Since the bruit over the head had not been detected before operation, a stethoscope was sterilized and placed upon the dura; a loud systolic bruit was audible. The dura was reflected from the brain and numerous adhesions between the dura and the pia-arachnoid were encountered. Some of the adhesions were flimsy and broke easily, others were so tough they required cutting. Only in one place was a vessel seen to pass directly from a cortical vessel to the dura. However, this anastomotic vessel was as large as the middle meningeal artery.

The surface of the brain thus exposed (Fig. 17) was largely covered by a tangle of reddish, tortuous, and pulsating vessels. Several of the largest vessels (8 to 10 mm. in diameter) extended from the depths of the lateral cerebral fissure obliquely across the field in the line of the rolandic fissure. Elsewhere over the surface the vessels were smaller. But anteriorly there was a compact mass, about 3.5 centimeters across, of small (1 to 2 mm.) vessels, which had an angiomatous appearance. The midcerebral artery, identified deep in lateral cerebral fissure, was fully three times its usual size at this location.

A faint thrill was detected by palpation of the large vessels and their thin walls made it possible to see blood swirling through them with each pulsation. Obviously these larger vessels were veins containing arterial blood. Compression of the right common or of both common carotid arteries in the neck caused an immediate decrease in the flow of blood through

these vessels and some even became promptly smaller but filled out again in a short time even though the pressure was maintained. No difference could be detected in the effects of compression of the right carotid from the effects of simultaneous compression of both carotid arteries. Compression of the left artery alone caused no visible change in the blood flow or in the size of the vessels.

The patient had two convulsive seizures during the time the cortex was exposed. They consisted of contraction of the left side of the face and upper extremity with a few clonic motions but no loss of consciousness. Preceding, during, or after the attacks no visible change in the vessels occurred. Both attacks stopped promptly after compression of the right carotid artery in the neck.

Faradic stimulation was applied to many points over all of the exposed vessels, even to those low in the lateral cerebral fissure, but no pain was elicited. The middle meningeal artery was widely pain sensitive.

No attempt was made to ligate any of the cortical vessels. A subtemporal decompression was made, a piece of the middle meningeal artery and dura was taken for microscopic study and the bone flap was replaced and sutured.

Microscopic examination of the section of the meningeal artery removed for study disclosed early arteriosclerotic changes but no other changes of note.

Recovery was uncomplicated and the patient was discharged 2 weeks after operation without medication for convulsions. The decompression was flat. In the year after operation he had two convulsions both following debauches of drinking. He considered himself improved because these convulsions were not severe and he had had six severe seizures in the year prior to operation.

The diagnosis should have been suspected before operation by the history of lateralized convulsive seizures and the curious vascular markings of the skull disclosed by roentgenogram, even though the bruit over the head was overlooked.

Two important facts were disclosed during the operation: one, that the flow of blood through the vessels of the aneurysm is definitely affected by compression of the carotid arteries in the neck though mostly by the one on the side of the lesion; the other, that the vessels of the aneurysm are not pain sensitive. Since this patient had no headache the latter finding would appear to have no great significance and in fact normal vessels in the same region have no pain sensitivity (20), yet it does have value in arriving at an interpretation of the localized headaches that have occurred in 2 other patients.

Because this case was much like that of Case 1 in which there was benefit from decompression alone it was thought best not to pursue the treatment here beyond simple decompression, at least to begin with. In the event of the return of frequent convulsions, both ligation of the right carotid arteries and roentgenotherapy will be advised.

DISCUSSION

The discussion will be limited to a consideration, principally, of the cerebral arteriovenous aneurysms which are typified by the 6 cases of this series and no attempt will be made to review exhaustively all the literature dealing with the subject. Also, since others have dealt fully with the differentiation and symptomatology of these and other vascular malformations of the head, emphasis will be put largely upon those aspects of the lesion—pathological, symptomatic, diagnostic, and therapeutic—that may supplement or refute past experiences and impressions.

THE NATURE AND SPECIFIC MANIFESTATIONS OF CEREBRAL ARTERIOVENOUS ANEURYSMS

Etiology. As pointed out by Dandy, it is unlikely that the arteriovenous aneurysms of the brain could result from trauma since the principal arteries and veins are not in juxtaposition as are the vessels of the extremities and elsewhere. In addition, the form in which these lesions occur is evidence of their congenital origin. They are composed of (a) an arterial side, the inlet, (b) a venous side, the outlet, and (c) multiple short communications or an interposing bed of racemose vessels. These latter vessels are malformations and are the counterpart of the normal capillary bed between arteries and veins. They have been found on microscopic examination, as in Case 4, to be both arteries and veins (3). Some authors have suspected that a venous malformation exists first which later becomes arterialized (1) but were this true arteries would not be expected in the "nests" of vessels just described.

The gross appearance. There is no mistaking these spectacular lesions when they are exposed at the operating table. One sees large, pulsating and tortuous veins, some a

centimeter or more in diameter, lying on the surface of the brain, and swirls of blood showing through their thin walls with each pulsation. The swirling appearance is due to the bright arterial blood mixing with darker venous blood and a dull red color is lent to the entire vessel which is the color neither of normal veins or arteries. The size of these veins varies, depending upon how directly the arteries empty into them. Thus, if the connecting vessels are few and of larger caliber, larger veins will result than if the arterial blood has first to pass through a greater number of smaller vessels. In the 4 cases subjected to exploratory operation not all the vessels were exposed in the operative fields but a comparison shows that in 2 of the cases in which the veins were largest there were fewer of the smaller vessels in evidence. It may be assumed that many veins both on the surface and in the substance of the brain undergo dilatation in the presence of an arteriovenous aneurysm because the arterial pressure must be dissipated in the venous system. As a matter of experience, it has been established that the external cerebral venous system is more characteristically implicated than the internal, though in Steinheil's case the veins of Galen were enlarged. The fact that the veins of the retina, in some cases, are distended indicates, however, that veins at a considerable distance are secondarily affected by the increase in the intracranial venous pressure. In Case 4 even the internal jugular vein was definitely large and pulsating.

The small connecting vessels also present an impressive sight in the form of tangled masses or "nests" of closely packed, pulsating arterioles and venules. On the whole, they have a redder color than the large veins but are usually still distinguishable from normal arteries. These more or less discrete masses of vessels have a tumorous appearance and no doubt have been the reason in the past for considering the lesions "angiomas." It is in these vessels that thrombosis and calcium deposits occur and doubtless changes of this nature predispose to rupture and hemorrhage.

The arteries that supply the fistula are themselves enlarged, sometimes to two or three times normal size. This is the result of a phenomenon which is spoken of as the "venafication" of the artery proximal to the fistula. The arterial wall thins out due to diminution of elastic tissue, loss of muscle fibers in the media, and stretching of the normal elements. It is supposed that the lowered peripheral resistance diminishes the degree of recoil and contraction of the artery and is the contributing factor in these atrophic changes (13). In Case 6 the mid-cerebral artery low in the lateral cerebral fissure was fully three times normal size and in the aneurysm of Case 3 the mid-cerebral artery was nearly as large as the internal carotid. In the illustration of Dennis' case (3), numerous arteries at the base of the brain were dilated but this is only to be expected since the carotid arteries in the neck and even the heart have been found to be enlarged (Cases 3, 4, and 5).

The cardiovascular effects. The effects upon the cardiovascular system of a cerebral arteriovenous aneurysm may be far reaching. This is a principle that has been well established by the now comparatively wide experience with arteriovenous fistulas elsewhere in the body in man, and also with experimental fistulas in lower animals. The effects, after the experimental production of arteriovenous fistulas, have been summarized admirably by Holman (12) and may be profitably quoted.

"The production of an arteriovenous fistula establishes two systems of circulating blood: (A) the heart-artery-capillary bed-vein system, and (B) the heart-artery-fistula vein system. The short-circuiting of a volume of blood through system (B), with its greatly reduced peripheral resistance, introduces a large factor of inefficiency into the circulatory system with particular reference to blood-pressure. The variable factors concerned in the maintenancy of blood-pressure are: (1) cardiac output, (2) total volume of circulating blood, (3) capacity of system, (4) peripheral resistance.

"The lowered peripheral resistance in the presence of a fistula is compensated by changes in the remaining three variable factors, and in this way only is an adequate blood-pressure level maintained.

"The volume of blood diverted and short-circuited through the lowered resistance of the fistula depends entirely on the size of the fistula, and the absence of any obstruction in the venous return flow to the heart proximal to the fistula. A small communication produces only slight changes, and these may not be detectable. Without present instruments of precision the slight alterations necessary to compensate for a small leak are not demonstrable, nor do

they produce any visible visceral changes. A slightly larger fistula may result in changes, only some of which are demonstrable. A fistula larger in size than the feeding artery, or large enough to divert a considerable flow back to the heart, invariably produces demonstrable changes, both immediate and remote. That these changes to a greater or lesser degree occur in the presence of every fistula, no matter what size, seems beyond question, the extent in each case depending entirely on the volume of blood diverted through the fistula.

"The immediate changes due to the production of a fistula are: (1) A fall in general arterial blood pressure affecting both systolic and diastolic levels; (2) an increase in pulse rate; (3) an increase in venous pressure, proximal as well as distal to the fistula, which is slight or pronounced, according to the size of the fistula.

"The remote effects following the production of a fistula are: (1) A permanent diversion of part of the blood volume from the circulatory system of heart-artery-capillary bed-vein into the second circulatory system of heart-artery-fistula vein. (2) A gradual increase in the amount of blood volume flowing through the new system, heart-artery-fistula vein, depending on the size of the fistula. (3) A gradually increasing vigor of heart action. (4) A gradually increasing total blood volume, proceeding *pari passu* with the amount of blood diverted through the fistula. (5) A gradual dilatation of the heart, and of the artery and vein proximal to the fistula, to accommodate this increasing flow of blood through the fistula. (6) Hypertrophy of the heart due to the increased work necessary to propel forward this increasing volume of blood flowing through it. (7) A gradual recovery from the lowered blood-pressure noted immediately after the formation of the fistula, the systolic equal or higher, the diastolic definitely lower than that existing before the formation of the fistula, thus producing a greatly increased pulse-pressure."

While many of the principles set forth in this summary are more or less applicable to the cerebral arteriovenous aneurysms under consideration, it is to be noted that on the whole the effects upon the cardiovascular system of the cerebral lesions are much less pronounced or dangerous to life than those that result from, say, an acquired aneurysm between the femoral artery and vein. The acquired fistulas of the carotid artery and cavernous sinus are more like the fistulas of the extremities in this respect. In one, the congenital origin of the lesion permits compensation from embryo, while in the other, compensation is more complicated. In addition, the amount of stress put upon the general cardiovascular system is directly proportional to the size of the artery and of its opening into the venous system. The mid-cerebral artery, which is the cerebral artery most frequently implicated, is several times smaller than an artery such as the femoral and the malformation of many small vessels between the cerebral artery and the cerebral veins has the effect of minimizing the size of the fistula.

In this series, Cases 2 and 4 had demonstrable enlargement of the heart with changes in their electrocardiographic records, while Case 6 had only electrocardiographic changes. Case 4, that of the 2½ year old child, showed the greatest changes in the cardiovascular system of all, and since there is no reason to assume that there is any essential difference between his aneurysm and the others it may be deducted either that, because of some unknown factors, he failed to compensate well or that in due time compensation might have been effective. This child also had the most pronounced elevation of pulse pressure in the series; Cases 1, 3, and 5 might be said to have slight elevation of pulse pressure. In Case 2, that of a 43 year old woman, the clinical picture was of hypertensive cardiovascular disease, and rather than attempt to explain her findings on the basis of the arteriovenous fistula it may be assumed that not only had she long since compensated for the fistula but had fortuitously developed hypertension. In the cases in which the carotid arteries in the neck were exposed (Cases 3, 4, and 5) these arteries were estimated to be enlarged; the finding was most pronounced in Case 4 and in the same case the internal jugular veins were also enlarged. The pulse rate was not unusual in any of the cases though in 4 the quality of the radial pulse was distinctly full and bounding and in Case 4 suggestive of a "Corrigan pulse."

The collateral circulation. The powerful stimulus to the development of a collateral arterial circulation imposed by an arteriovenous fistula is evident in individuals having cerebral arteriovenous aneurysms. Enlarged, tortuous and pulsating arteries of the scalp as well as enlarged middle meningeal arteries have been observed commonly in these individuals. In Cases 1, 3, 4, and 5 the arteries of the scalp, and in Cases 1, 2, 3, and 6 the middle meningeal arteries exposed at operation

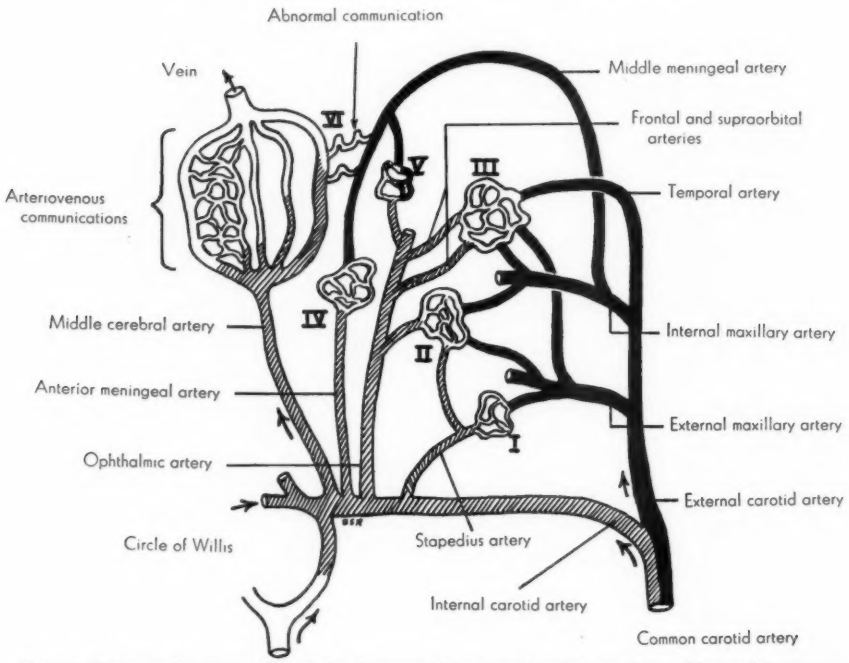


Fig. 18. Schema of collateral circulation between the external and internal carotid arterial systems. *I*, Facial region; *II*, orbital region; *III*, supraorbital region; *IV*, dura of frontal fossa; *V*, variable connection between the middle meningeal and ophthalmic arteries; *VI*, abnormal communications between the dural and pial arteries.

were distinctly enlarged. In Case 3 the foramen spinosum on the side of the lesion was shown on roentgenogram to be enlarged (Fig. 4b) and in Case 4 this foramen was found at autopsy to be twice as large as its mate.

On first thought it is difficult to see how there can be readily established a collateral circulation between the branches of the external and internal carotid arteries since the two are often thought of as distinct and separate arterial systems. But the superficial temporal artery, a terminal branch of the external carotid artery, has rich anastomosis not only with the corresponding artery from the opposite side of the head and with the occipital arteries but also with the supraorbital and frontal arteries which are terminal branches of the ophthalmic artery, itself a branch of the internal carotid (Fig. 18). Many other anastomotic relationships exist with the branches of the internal carotid in the orbital region, and also with the branches of the external carotid in the facial region. With the exception of the central artery of the retina, all the branches of the ophthalmic artery communicate with some division of the external carotid, the principal ones being the external maxillary, the internal maxillary, and the superficial temporal arteries. The middle meningeal artery, a secondary branch of the external carotid artery, anastomoses with the anterior meningeal arteries, one of which originates directly from the internal carotid and the others from ethmoidal branches of the ophthalmic artery. Wolff has called attention also to the communication of branches of the external carotid in the face with the stapedius artery, a branch of the internal carotid.

Connection may exist between the middle meningeal and the ophthalmic arteries through a variety of anomalies, for in some lower animals the ophthalmic arises wholly from the meningeal and vestiges of this arrangement persist in man (27, 32).

In addition to the collateral circulation between the external and internal carotids which utilizes the normal arrangement, often there is found the unique development of vessels that pass directly from the cerebral aneurysm to the overlying dura and the meningeal arteries. In all of the 4 cases in which cerebral exploration was performed and in the case with postmortem examination, these anastomotic vessels were seen. In Case 6 but one such vessel was encountered whereas in the others a number of short, and sometimes large calibered, aberrant vessels were present.

The external carotid arteries of the two sides are connected by numerous unions between the lingual, external, maxillary, occipital, posterior auricular and ascending pharyngeal arteries which make up abundant peribuccal and peripharyngeal circles. The external carotid arteries also possess efficient anastomotic communication with the thyrocervical trunks via the thyroid arteries principally and with the costocervical trunks via the occipital arteries. Case 3 exemplifies the most extensive interruption of the blood supply to the brain by ligation of the internal and external carotid arteries on each side of the neck and one superior thyroid artery. Here it is to be assumed that while the vertebral arteries comprise the principal supply to the brain it must still receive some arterial blood through the internal and external carotid arteries whose more distal branches communicate with branches of the thyrocervical and costocervical trunks.

The bruit and thrill. The bruit and thrill accompanying arteriovenous aneurysms have been attributed to various causes but the most acceptable explanation is that they result from vibration of the walls of the vessels. The vibration is produced by alternating currents of blood under high and low pressure (13). In all 6 of the cases of this series a bruit was detected first or last by auscultation over the head and neck. In the first 2 cases, due to what Cushing and Bailey (3) termed a "strange human frailty," auscultation of the skull was not a part of the preoperative examination and the bruit was not heard until after the nature of the lesion had been established by operation. In the next 3 cases auscultation was a part of the examination of the head and the bruit was readily detected. But in the sixth case, although several observers auscultated the head, the bruit was overlooked. Doubtless, the size and the individual arrangement of a cerebral arteriovenous fistula has some effect upon the intensity of the bruit, yet it is likely that if listened for carefully, a bruit will always be detected somewhere over the head when the lesion is present. It was loudest, in all 6 cases, in that region of the head that overlay the lesion, but in 2, it was also heard over other parts of the cranium. The bruit heard over the eyeballs was sometimes more distinct than that heard over the skull, although in Case 2 it was heard only faintly over the homolateral eyeball. A bruit was also heard over the carotid arteries in the neck in 5 cases; in the 2 children it was present over both sides but loudest on the side of the lesion.

The presence of a bruit over the carotid arteries in the neck is probably the result of the transmission through the carotids of the sound which originates in the vessels of the cerebral aneurysm. The jugular veins could contribute little or nothing to the sound since the internal jugular vein exposed in 3 individuals was found in only 1 to be unusually large and tense. In this latter case the bruit in the neck disappeared after ligation of the carotid alone.

The bruit heard over the eyeballs must be similarly dependent upon transmission of the sound through blood vessels of the orbit. The ocular bruit, and also the pulsating exophthalmos, associated with the fistulas between the carotid artery and cavernous sinus appears to be dependent principally upon the veins of the complex while the ocular bruit associated with the cerebral lesions under discussion are dependent in large part upon the arteries of the orbit. Furthermore, the arterial collateral circulation through the orbit, already discussed, probably contributes chiefly to the transmission of the bruit. This conclusion is suggested principally by the fact that occlusion of the internal and external carotid arteries on one side (Cases 3, 4, and 5) caused almost complete disappearance of the bruit over the homolateral eyeball but did not affect that heard over the contralateral globe. Additional and perhaps more conclusive evidence was afforded by the finding, in Case 3, that liga-

TABLE I.—ANALYSIS OF THE AUTHOR'S SIX CASES OF CEREBRAL ARTERIOVENOUS ANEURYSM

	Frank B., No. 137699 41 yrs.—M.	Helen R., No. 127311 43 yrs.—F.	Mike B., No. 146422 20 yrs.—M.	George S., No. 221823 3 yrs.—M.	Marie L., No. 227011 14 yrs.—F.	Edward R., No. 205151 42 yrs.—M.
History of trauma	No	No	No	Questionable	No	No
Site of lesion	Left fronto-parietal	Right parietal	Right fronto-parietal	Right fronto-parietal	Left parietal	Right parietal
First symptom and age of onset	Generalized headache at 4 yrs.	Paresthesias of left hand at 40 yrs.	Convulsions at 14 yrs.	Transient left hemiplegia at 2½ yrs.	Hemiparesis since birth	Convulsions at 36 yrs.
Symptoms (and age of onset): Convulsions	Generalized, averaged 2 a year. Began at 26	Left sided petit and grand mal, at 41	Left sided petit and grand mal	None	Only after ligation of carotid artery	Generalized, beginning on left side
Symptoms (and age of onset): Palsy	No	No	No	Left hemiparesis	Right hemiparesis	No
Symptoms (and age of onset): Paresthesias	No	Left hand at 40	No	?	No	Left hand and face
Symptoms (and age of onset): Headache	Generalized at 4. Left frontal, began at 38	No	No	No	Daily left frontal. Began 13 yrs.	No
Time of convulsions	3 nocturnal. Others diurnal	Diurnal	1/4 nocturnal. 3/4 diurnal	0	0	Diurnal
Increased vascularity of scalp	Yes	No	Yes	Yes	Yes	No
Mental changes	None	Panic state. Paranoid psychosis	None	None	None	None
Bruit and location heard	Left frontal area. Both eyeballs. Not detected preoperatively	Right frontal area. Right eyeball. Right side neck. Not detected preoperatively	Right fronto-parietal. Both eyeballs. Right side neck. Detected preoperatively	Entire head. Both eyeballs. Both sides of neck. Detected preoperatively	Entire head (lt. > rt.). Both eyeballs. Both sides of neck (lt.>rt.). Detected preoperatively	Right fronto-parietal. Both eyeballs. Over right side of neck. Not detected preoperatively
Cardiovascular changes P. B. P. E. K. G.*	BP 118/70. P 70. Pulse quality normal. Heart sounds normal. Heart on x-ray normal. EKG not done	BP 165/108. P 80. Pulse quality bounding. Heart sounds normal. Heart on x-ray: slight left enlargement. EKG: left ventricular preponderance	BP 110/66. P 75. Pulse quality full. Heart sounds: faint systolic murmur. Heart on x-ray normal. EKG normal	BP 104/70. P 70. Pulse quality bounding. Heart sounds: systolic murmur. Heart on x-ray: enlarged to left and enlarged superior vena cava. EKG: left ventricular preponderance	BP 100/50. P 90. Pulse quality bounding. Heart sounds normal. Heart on x-ray normal. EKG normal	BP 122/80. P 80. Pulse quality normal. Heart sounds normal. Heart on x-ray: slightly enlarged to left. EKG: left ventricular preponderance
Optic fundi	Slight papilledema. Full vessels bilaterally	Full, tortuous vessels right side	Full tortuous vessels on right side	Full, tortuous vessels both rt.>lt.	Vessels full and tortuous on left	Normal
X-ray of skull: Increased vascularity of skull	Yes	Yes	Yes	Slight (large head)	Yes (slight enlarged head)	Yes
X-ray of skull: Erosions due to pressure of vessels	Yes	No	Yes	No	Yes	Yes
X-ray of skull: Calcification in lesion	Yes	No	No	No	Yes	No
Spinal fluid	Pressure 220 mm. Total protein, .050 gm. %	Not studied	Pressure 200 mm. Total protein, .020 grams %	Normal pressure. Total protein, .030 grams %	Normal pressure. Total protein, .040 grams %	Normal pressure. Total protein, .040 grams %
Cerebral arteriography	0	No	Yes	Yes	Unsatisfactory	No
Encephalogram or ventriculogram	Ventriculogram. Depression of left frontal horn	Ventriculogram. Irregularity of body of right lateral ventricle	Encephalogram. Deformity of right ventricle and slight shift to left. Mottling over right hemisphere	Encephalogram. Depression of right and slight shift to left. Mottling over right hemisphere	Encephalogram. Poor filling and irregularity of left ventricle. Mottling over left hemisphere	Ventriculogram. Small depressed ventricle, right

*P., pulse; B.P., blood pressure; E.K.G., electrocardiogram.

TABLE I.—ANALYSIS OF THE AUTHOR'S SIX CASES OF CEREBRAL ARTERIOVENOUS ANEURYSM
Continued

		Frank B., No. 137699 41 yrs.—M.	Helen R., No. 127311 43 yrs.—F.	Mike B., No. 146422 20 yrs.—M.	George S., No. 221823 3 yrs.—M.	Marie L., No. 227011 14 yrs.—F.	Edward R., No. 205151 42 yrs.—M.
Operation	Occlusion of carotid arteries	No	No	Right common and external arteries 3-23-1939. Left internal carotid 11-24-1939. Left external carotid, 12-7-1939	Right common and external carotid 2-15-1939. Left internal and external carotids 4-27-1940	Left common and external carotids 4-29-1939	No
	Exploration and subtemporal decompression	7-20-1936	9-1-1936	10-10-1936	No	No	11-15-1939
X-ray therapy		1,050 r units (inadequate)	10,200 r units over 18 mos.	13,200 r units over 28 mos.	0	0	0
Result of treatment		Fewer convulsions. Headaches stopped for 1 yr., then recurred with less severity over left frontal area	No improvement in mental state. Fewer convulsions	Cessation of grand mal convulsions. Fewer and slighter petit mal attacks	No improvement except diminution in size of heart after first operation. Death 3rd day after 2nd operation. Autopsy	Relief of headache	Fewer convulsions

*P., pulse; B.P., blood pressure; E.K.G., electrocardiogram.

tion of the contralateral internal carotid caused marked diminution in the cephalic bruit but an increase in the bruit over the eyeball on that side; this bruit was greatly diminished, however, when the common carotid on that side was occluded, thus shutting off the principal supply to the external carotid artery. The shifting or intensification of the bruit to the unaffected side is mentioned by Singleton in his experiences in ligation of the carotids for intracranial arteriovenous fistulas.

It is an interesting fact that in none of the cases of this series did the patients complain of tinnitus or noise in the head prior to operation, nor could they detect any noise when told that one was present. Case 4, the child of 2½ years, may possibly be an exception. In cases reported elsewhere (1, 3), some patients have been aware of the bruit and it is probable that the location of the aneurysm has some influence upon this; the nearer to the petrous bone the more likely the patient is to be aware of it. Brock and Dyke ascribed the tinnitus in one of their patients to the auditory perception of the systolic bruit in the adjacent enlarged temporal artery. It was suggested by Cushing and Bailey (3) as quite conceivable that a decompression operation might serve to accentuate a sound which would otherwise be dampened by a closed cranial chamber, and this seems to have been the case in the last patient who detected a faint bruit for the first time after cranial exploration and subtemporal decompression.

The location of the aneurysms. In this series, all the aneurysms have appeared to be the result of an anomalous formation involving principally the mid-cerebral artery. In a majority of the collected cases the mid-cerebral artery has been concerned but the malformation may occur in arteries anywhere in the brain. The lesion's next most frequent location has been the occipital lobe, probably the result of malformation of the posterior cerebral artery, and other rarer locations have been the cerebellum (3, 4, 17, 34),[1] the corpus callosum (5), the corpus striatum (28), and the midbrain (1). In 1 case (33), besides the cerebellar lesion, there was a second and similar lesion in the parietal lobe.

THE INCIDENCE OF ARTERIOVENOUS ANEURYSMS OF THE BRAIN

Congenital arteriovenous aneurysms in all locations of the brain are said by Dandy to have a frequency of 0.5 to 1 per cent in clinics where neurological material is concentrated. In Cushing's (2) summary of 2,023 verified brain tumors the frequency of "angioma arteriole" was about 0.5 of 1 per cent. The comparatively low incidence of the lesion neces-

[1]See footnote on following page.

sarily limits any one individual's experience with it and it is a fortunate occurrence that in the short space of 4 years the 6 cases of this series (and 1 additional case[1] not included in this series) should have come under the author's observation and been available for frequent observations during that time.

Males seem to develop these lesions more often than females in a ratio of about 3 to 1; in this series the ratio is 2 to 1.

THE SYMPTOMS AND SIGNS OF CEREBRAL ARTERIOVENOUS ANEURYSM (TABLE 1)

Onset. It is a striking fact that although there is sufficient reason to believe the lesions to be congenital (24), symptoms often do not make their appearance or at least do not come to serious attention until comparatively late. Some have thought this to be evidence against their congenital origin. It suggests, rather, that the explanation for the tardy symptoms lies in the hypertrophic and the premature degenerative changes constantly occurring in the vessels of the lesion which in turn are accompanied by hemorrhage, by destruction of nervous tissue and possibly by an expansion in the volume of the vessels involved. Trauma might well serve to increase the size or produce other changes in a lesion already present just as trauma has been seen to enhance the growth of a cirsoid aneurysm of the scalp (7). Cushing and Bailey (3) stated that to their knowledge the lesion had not been observed in infancy, yet one of the cases reported here is that of a child, 2½ years old, and the author has examined but does not have complete records of an 11 months' old baby whose symptoms and signs were undoubtedly those of a right cerebral arteriovenous aneurysm.

First symptoms and the age of their appearance in the cases of this series are listed as follows: Case 1, headaches since the age of 4 and first convulsion at 26; Case 2, attacks of paresthesia in the left upper extremity at 40; Case 3, generalized convulsion at 14; Case 4, transitory left hemiparesis at 2½; Case 5, right sided weakness since infancy; Case 6, convulsive seizure beginning in the left upper extremity at 36.

[1]One case of congenital arteriovenous aneurysm of the cerebellum has been encountered by the author and exposed at operation but is not included in this report which deals only with the cerebral lesions.

Convulsions. Convulsions were the first important symptom in but 3 of the cases though in all 6 convulsions eventually occurred. In all instances there was some clue before, during, or after attacks, as to the side of the body more affected, but there was no distinctive feature about the attacks that would stamp them as different from those caused by some other lesion in the parietal region of the brain. However, convulsions are not necessarily an accompaniment of any lesion that involves the paracentral area of the cerebrum, and it would be erroneous to insist upon the occurrence of convulsions for the diagnosis of a cerebral arteriovenous aneurysm.

Focal signs and symptoms. Transient hemiparesis, as occurred in Case 4, has been mentioned commonly in the reports of others, and the most reasonable explanation for such events is thrombosis or hemorrhage. A lumbar puncture performed within a few hours after the rapid development of hemiplegia in this patient failed to show any abnormality in the fluid; while thrombosis appears to be the most plausible explanation, no thrombosed vessels could be discovered on final examination of the brain. Doubtless the early appearance of unprogressive hemiparesis in Case 5 was the result of thrombosis or hemorrhage of the lesion in babyhood.

Other focal symptoms and signs that might reasonably be expected to occur with arteriovenous aneurysms of the cerebrum are sensory disturbances, aphasia (if the lesion is on the proper side) and visual perimetric defects. These were not present as constant findings in any of the cases though in Case 5 following ligation of the carotids, there were three convulsions which were preceded by aphasia and a right homonymous hemianopsia.

Headache. Headache was not an outstanding symptom in the records of the cases that have been reported by others and often, when mentioned, it was not qualified or thought important enough to ascribe to any particular mechanism. Increased intracranial pressure was perhaps the explanation of some instances of headache but not all, for intracranial hypertension was a comparatively infrequent development. Convulsions and subarachnoid hemorrhage were the causes of headache in

other cases. However, there is a group of cases remaining in which the headache cannot be ascribed to any one of these. In the light of increasing information with regard to the pain sensitivity of various intracranial and extracranial structures, and the mechanism by which headache can occur (20, 26), it may be profitable to consider the headaches associated with cerebral arteriovenous aneurysms not the result of the causes just mentioned.

The headaches referred to are typified by those described in Cases 1 and 5. They occurred periodically, sometimes daily, and usually appeared very soon after rising in the morning; they were localized over the frontotemporal region of the head on the same side as the aneurysm; they had a dull, painful, throbbing character and were associated with nausea; they lasted for several hours at a time. In Case 1 the headache was preceded by pain which began low in the neck and progressed upward into the side of the face and finally localized in the head. A case fully described by Brock and Dyke was very like these and the headache was said to be migraine but thought not to be related to the cerebral arteriovenous aneurysm. Certainly, this type of headache is in every way comparable to migraine and it must be other than chance that the pain is limited to, or at least more severe on, the side of the aneurysm.

The headache in migraine results from distention largely of the extracranial and the middle meningeal arteries (9). Since these vessels have all been shown, in the previous discussion, to be abnormally large and more particularly so on the side of the lesion in cases of cerebral arteriovenous aneurysm, it is fair to assume that their dilatation is responsible for the type of pain under consideration. The presence of headache at one time and not at another probably depended upon factors influencing vascular tone in general; for example, the headaches were matutinal which is also characteristic for migraine.

Additional facts in the cases to support the analogy are present. In Case 1 the headaches were greatly improved after a decompression operation in which the middle meningeal artery necessarily was transected low in the temporal fossa. Also, several of the abnormal communicating arteries between the aneurysm and the middle meningeal artery were severed. Since the area of the decompression gave little or no evidence of the presence of increased intracranial pressure, it is reasonable to conclude that interruption of the middle meningeal artery and its abnormal connections with the aneurysm was responsible for the relief of headache. Transection of the middle meningeal artery near the foramen spinosum in patients with migraine has served to diminish their pain until regeneration of the artery or its nerve supply permitted a return (9). The developments in Case 5 further support this belief for here the ligation of the external and internal carotid arteries on the side of the lesion served to improve the headaches greatly. On the basis of the diminution in the intensity of the bruit over the homolateral eyeball but not elsewhere over the head, the inference is that the vascularity of the branches of the external carotid was proportionately more affected than was the aneurysm itself by the combined ligation.

It is unlikely that the dilatation of the cerebral arteries, per se, plays any rôle in this migrainous headache. Normally the arteries and veins over the lateral and superior convexity of the brain are insensitive to pain when stimulated with faradic current (20) and it was found in Case 6 that stimulation of the abnormal vessels of the aneurysm in the same regions over the cortex failed to cause pain. There is still to be considered the possibility of the dilatation of the intracranial portion of the internal carotid and the proximal one to two centimeters of the mid-cerebral arteries as a contributing factor to the headache in these cases, for these vessels are normally pain sensitive in this area. The pain resulting from their stimulation, however, has a localization in and about the homolateral eye which is somewhat different from the frontotemporal pain following stimulation of the middle meningeal and temporal arteries and the location of pain in the cases under consideration was largely frontotemporal (20). Also, the pain arising from the extracranial and meningeal arteries in migraine is relieved by ergotamine (9) while it is not so certain that the pain arising from the dilatation of cerebral

arteries is relieved by this drug. In Case 5 the injection of half an ampul (.25 mgm.) of ergotamine stopped the headache on the one occasion when it was tried.

The possible contribution to headache made by traction of the abnormally large superior cerebral veins upon the sagittal sinus can probably be dismissed on the grounds that the various measures mentioned as beneficial would have least effect on these veins.

Dandy's explanation for the localized headache in one of his cases was "contact of the vascular bed with the meninges." The exact mechanism he meant to imply is not clear. No part of the meninges including the pia, arachnoid and dura in this region is pain sensitive except the meningeal artery. In the case reported by Hyland and Douglas, they state "it might be possible to explain the headaches on the basis of increased blood flow transmitted to the vessels of the tumor, leading to compression and distortion of vessels in the portion of the meninges which were observed to be adherent to the tumor." Occasionally pressure upon the meningeal artery by an intracranial tumor may be sufficient to cause pain in the frontotemporoparietal region. But a more cogent explanation for the headache is the dilatation which occurs in the meningeal artery as a result of direct and indirect vascular connections with the aneurysm.

Increased intracranial pressure and ophthalmological signs. Increased intracranial pressure has occurred in a conspicuously low percentage of the cases of cerebral arteriovenous aneurysm that have been reported. The spinal fluid pressure was in the neighborhood of 200 millimeters of water in Cases 1 and 3 and there was fullness of the optic disks in Case 1 but none of this series had an outspoken increase in pressure. This is significant when the large size of the lesion, sufficient to distort the ventricles, is considered. The intracranial adjustment, however, begins early in life, and the changes in the aneurysm are usually gradual. It is likely that at various periods in the lives of some of these patients, perhaps following thrombosis or hemorrhage and readjustment of the aneurysm, there have been transitory periods of increased pressure.

The presence of full retinal vessels and low grade papilledema may have a different significance than is usually implied in the presence of intracranial space-occupying lesions. In the cases under discussion the total intracranial blood volume is increased and the venous pressure is high. Even though there may be sufficient readjustment of the brain to minimize or counteract sustained increased intracranial pressure, both the veins and the arteries of the eye may be enlarged. The veins enlarge due to increased venous pressure and the arteries enlarge as a part of the regional arterial dilatation discussed earlier. Associated changes in the appearance of the disk itself therefore may be the result purely of local vascular changes, such as local venous stasis. Papilledema is a common accompaniment of the venous stasis that occurs with fistulas between the carotid artery and cavernous sinus. In Case 1 there was a slight bilateral papilledema, less than one diopter, and more pronounced on side of lesion. In this case also, the retinal veins as well as the arteries were full, tortuous, and sometimes difficult to distinguish from each other. In Cases 2, 3, and 5 the retinal vessels had a similar appearance on the side of the aneurysm while in Case 4 the change was present in both eyes.

None of the 6 individuals had exophthalmos or pulsating eyeballs and this may usually be relied upon to differentiate the congenital cerebral aneurysms from the acquired fistulas of the carotid artery and cavernous sinus which characteristically cause unilateral pulsating exophthalmos. However, slight exophthalmos without pulsation of the eyeball sometimes greater on the side of the lesion has been reported in association with the cerebral aneurysms (1) and Cushing and Bailey (3) were impressed with its incidence in a third of their cases. They concluded that both the exophthalmos and the full retinal vessels were the result of "pumping arterial blood directly into the cerebral veins, a condition which is, in the nature of things, more marked in the vicinity of the lesion." Pulsating exophthalmos in connection with a cerebral arteriovenous aneurysm reported by Rotgans and Winckler was said by Cushing and Bailey (3) to be the only instance of its kind.

TABLE II.—ABNORMALITIES IN ROENTGENOGRAMS OF THE SKULL

Case No.	Side of lesion	Enlarged head	Accentuated vascularity of the skull	Enlarged grooves of middle meningeal artery	Enlarged foramen spinosum	Signs of increased intracranial pressure	Erosions—pressure of vessels of aneurysm	Intracranial calcification
1	Left	No	Both sides. Greater in front and on left	Left	Not examined	Thin posterior clinoids	Left parietal	Left fronto-parietal cortex. Left internal carotid artery
2	Right	No	Marked on both sides	Right	No change	Slight "digitation" and thin posterior clinoids	Right parietal	None
3	Right	No	Moderate on both sides	Both sides. Right>left	Right>left	Slight "digitation" and thin posterior clinoids	Right parietal	None
4	Right	Yes	Slight on both sides. Right>left	Right	No change seen (right larger at autopsy)	None	None	None
5	Left	?	Bifrontal	Both sides. Left>right	Not examined	None	Left parieto-temporal	Left parietal, subcortical
6	Right	No	Both sides. Greater in front and on right	Both sides. Right>left	No change	None	Right parietal	None

AIDS TO DIAGNOSIS

Spinal fluid. Spinal fluid examination has a limited value in the diagnosis of cerebral arteriovenous aneurysms since there was nothing constant in the findings in all cases. In Cases 1 and 3 the resting pressure of the fluid was slightly elevated (in the neighborhood of 200 millimeters of water), but in only one of these was the total protein content elevated (.050 gram per cent). In Cases 5 and 6 the total protein was .040 gram per cent which is considered to be the upper limits of the normal value. In Case 4 the spinal fluid, collected shortly after the advent of spontaneous hemiparesis, failed to show any abnormalities. It should be mentioned, however, that since these aneurysms are prone to rupture, the finding of blood in the cerebrospinal fluid should always raise the question of their presence.

Roentgenography of the skull. A study of the roentgenograms of the skull in the 6 cases of this series resulted in the discovery that some changes due to the presence of a cerebral arteriovenous aneurysm were present in all cases (Table II). Brock and Dyke in a similar analysis of 5 cases found some distinctive changes in the roentgenograms of all. The important abnormalities in this series were: (a) Questionable or slight signs of increased intracranial pressure, present in Cases 1 and 2. (b) Increased vascularity of the skull (enlarged diploe), present in Cases 1, 2, 3, 4, 5, and 6. (c) Enlarged channels for the middle meningeal arteries, present in Cases 1, 2, 3, 4, 5, and 6. Enlargement of the foramen spinosum, present in Case 3. (d) Local atrophy due to pressure of the aneurysm, present in Cases 1, 2, 3, 5, and 6. (e) Calcification in the vessels of the aneurysm, present in Cases 1 and 5. (f) Overgrowth of the cranium causing large head, present in Cases 4 and possibly 5.

The enlarged diploe are manifestations of the general increase in venous pressure of the region. The increased pressure in the cerebral veins and sinuses is transmitted directly to these venous channels in the skull and an example of the degree of the pressure is the force with which blood spurted from the temporal diploic vein at operation in Case 3. Most of these changes in the skull demonstrable on the roentgenogram have been mentioned by others (1, 18), but the localized, often oval shaped, areas of rarefaction due to erosion of the inner table of the skull overlying the abnormally large, pulsating vessels of the aneurysm have received little attention. These areas were present in 5 of the cases of this series and in 4 the relation of the depressions to large vessels was demonstrated at operation.

Possible enlargement of the foramen spinosum as a result of dilatation of the middle meningeal artery could not be determined

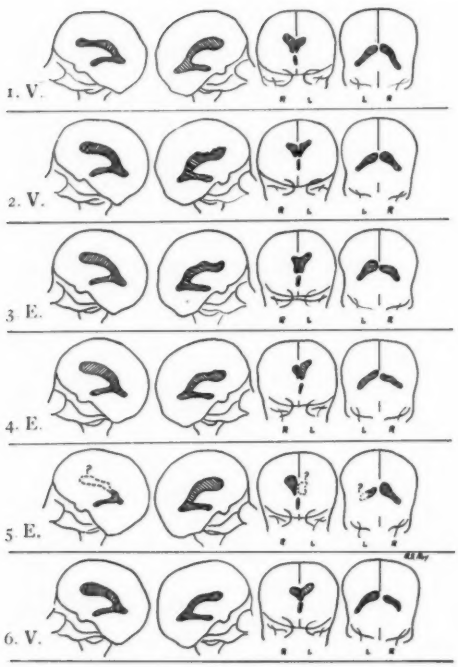


Fig. 19. Composite of ventricular configurations demonstrated by injection of air in the 6 cases of this series. *V*, Indicates ventriculography; *E*, indicates encephalography. Note that there is some slight abnormality present in all cases.

from the plates in all the cases but was observed to be present in striking degree in Case 3 (see Fig. 4b). A similar finding has been reported by Lindblom. Enlargement of the cranium has not been mentioned by others as a secondary feature of the cerebral vascular malformations and it was not evident in the 4 oldest patients of this series but in the 2 children, Cases 4 and possibly 5, there was enlargement of the head. This enlargement did not appear to be the result of increased intracranial pressure but probably was a form of overgrowth comparable to that seen in the extremities in the presence of arteriovenous fistulas. Thickening of the skull occurring in 2 patients as a result of "over-vascularization" was mentioned by Brock and Dyke.

Air studies—encephalography and ventriculography (see Fig. 19). In this series ventriculography was performed upon 3 of the patients and encephalography upon 3. In every instance there was some distortion or displacement in the ventricles although the defects were not always pronounced. The irregularity in the ventricular outline, as it occurred in Case 2, is probably due to enlarged aneurysmal vessels in the wall of the ventricle at that point and gives a clue to the depth of a lesion which appeared at operation to be largely on the surface of the brain. The distinct shift of the ventricles to the side opposite the lesion occurred in Cases 3 and 4 even in the absence of increased intracranial pressure. Scanty amounts of air appeared in the homolateral ventricle in Case 5 and while this may have been due to faulty manipulation of the head at the time of taking the roentgenogram, it may very possibly be that the ventricular lumen on that side is extensively encroached upon by enlarged vessels of the aneurysm.

Perhaps encephalography is a safer and even more advantageous procedure to employ in these cases than ventriculography. Certainly the introduction of a ventricular needle into one of the vessels of the aneurysm might lead to speedy disaster while encephalography has the advantage of sometimes showing abnormal shadows in the sulci of the region of the aneurysm as seen in Cases 4 and 5.

Electroencephalography. Records of the cortical electrical activity were made in Cases 3 and 4 and gross pathological waves were recorded from all parts of the cerebrum in both. The changes were greatest over the frontal areas but approximately equal on the two sides. The test was not helpful in localizing the lesion but it may be with increased experience in use of the instrument and interpretation of its records, more valuable information in these cases will be obtained.

Cerebral angiography. Both thorotrast (thorium dioxide solution) and diodrast (10) have been used for purposes of outlining the intracranial vasculature. There has been ample warning of the danger of the use of the former (21), yet some investigators (33) hold that the radioactive material in amounts used in the cases of this series is well within the limits of theoretical safety. There were no immediate ill effects from the use of thorotrast in 3 cases and sections of the liver showing the

presence of the substance 15 months after injection disclosed no change in the adjacent cells. Diodrast, although lacking in radioactivity, has been found occasionally to produce undesirable cerebral reactions and there is probably greater danger of its producing thrombosis of the carotid or its branches. The routine use of either substance to demonstrate the more common forms of intracranial pathology is not justified but its occasional use is warranted in cases of arteriovenous aneurysm in which it is desirable to show the exact location and extent of the lesion.

Thorium was injected three times (Cases 3, 4 and 5) and 35 per cent diodrast once (Case 4) in the cases of this series. In Case 5 no shadow was obtained, perhaps because of faulty technique but possibly because of increased circulation time in the brain. Usually the radiopaque substance outlines only the cerebral vessels of the side on which the injection is performed as seen in Figure 10. But in Case 3, 8 months after the carotid arteries on the side of the aneurysm were ligated, thorotrast injected into the opposite carotid crossed over through the anterior communicating artery and outlined the lesion as shown in Figure 6. In Case 4 diodrast injected on the side opposite the aneurysm, after ligation of the homolateral carotids, was found not only to outline the normal cerebral arteries of that side but also to cross over and outline the lesion. It would be interesting to know in these cases if injection of the radiopaque material on the contralateral side would have outlined the lesion had the homolateral carotids not been occluded, for it would supply additional information about the cerebral circulation in the presence of the aneurysm.

THERAPEUTIC CONSIDERATIONS

The very nature of cerebral arteriovenous aneurysms makes it impossible to settle upon a completely satisfactory method of treatment. The ofttimes unhappy experiences in the use of various forms of treatment have introduced a note of caution and indeed the question has been raised whether any treatment should be attempted. Because there is the threatening possibility that persons with this lesion may die from spontaneous rupture of one of its vessels (41 per cent quoted by Dandy), especially during a convulsion, there is an incentive to utilize whatever reasonably may offer benefit. The experience with varied treatment resulting in some benefit in symptoms in the cases of this series, has seemed to justify this attitude.

Decompression operation combined with exploration. This operation was performed in 4 patients (Cases 1, 2, 3, and 6). No attempt was made in any to remove or ligate the cerebral vessels of the aneurysm. However, some of the abnormal vessels that anastomosed directly with the dural (middle meningeal) arteries were transected and also the main trunk of the enlarged middle meningeal artery was interrupted low in the temporal fossa, as a part of the decompression. A moderate sized decompression beneath temporal muscle was produced even though there were no frank signs of increased intracranial pressure.

The value of this type of operative procedure is that the nature of the lesion can be positively identified; some of the arterial supply to the aneurysm through the middle meningeal artery can be eliminated; the interruption of the middle meningeal artery may be beneficial in those with local headache; the decompression relieves whatever co-existent or transitory increased intracranial pressure there may be; and subsequent roentgenotherapy may be more effectively directed at the lesion through the defect in the skull, though the latter is by no means certain.

The disadvantage and danger of an osteoplastic operation or even of a simple subtemporal decompression is the threat of serious hemorrhage, particularly from inadvertent tearing of the large vessels of the aneurysm.

Ligation of the carotid arteries. This procedure has been performed in Cases 3, 4, and 5 of the series. In all 3 patients the common and external carotid arteries on the side of the aneurysm were ligated and in addition, in 2 (Cases 3 and 4), the internal and external carotids on the opposite side were ligated 8 months and 15 months later.

The value of this type of operative procedure is that the arterial supply, and thus the tension, of the vessels of the aneurysm is diminished. It may be effective in lessening

the danger of spontaneous rupture and be conducive to the spontaneous occlusion of some of the vessels. The favorable effect upon the heart in minimizing the arterial supply to the lesion is well demonstrated in Case 4 (see Figs. 9a and b). An unanticipated benefit that resulted from operation was the marked improvement in headache in Case 5, the only one of these 3 with headache to begin with.

The hope, when the carotids are occluded, is that just enough arterial blood will be diverted from the lesion to accomplish the desired results but not so much that serious anoxia of the brain will ensue. Because of the extensive collateral circulation, the factor of safety in the ligation of any single artery is greater than in persons without arteriovenous communications. The ill repute of ligation of the carotids as the cause of hemiplegia and death is the result largely of ligations for infections, injury, and malignancy in the neck and face (6, 14, 18), states not at all comparable to the arteriovenous aneurysm. Watson and Silverstone report a 55 per cent mortality in 20 patients having unilateral ligation of the common carotid for carcinoma of the head and neck whereas in Matas' series of 80 occlusions of the common and internal carotids (presumably all for intracranial arteriovenous anomalies) the mortality was 7.5 per cent.

Occlusion of the common carotid alone is less dangerous but at the same time less effective in diminishing the arterial supply to the aneurysm than occlusion of the internal carotid. This is due to what has been spoken of as "reversal of blood flow" in the external carotid after ligation of the common carotid. Dorrance estimated that ligation of the common carotid alone removed but 50 per cent of the blood flow through the internal carotid. Keegan found that ligation of the common carotid alone was followed in a few weeks by enlargement of the external carotid, "necessitating later ligation of the internal carotid with more lasting benefit." For more complete effects therefore it is necessary to ligate the external or the internal carotid subsequently.

Occlusion of the internal carotid alone, because of its anatomical arrangement, is sometimes not easily or safely rectified if it is found necessary to remove the ligature on the development of late cerebral disturbance. Also, occlusion of the internal carotid alone, in an effort to diminish extensively the supply to the aneurysm, as shown in the second operation in Case 3, disregards the rich collateral supply to the aneurysm via the external carotid through numerous anastomoses (see Fig. 18). However, the lesson to be learned from the experience in Case 4 is that simultaneous ligation of the internal and external carotids carries more hazard than successive ligation with an interval sufficiently long to permit accommodation.

The frequency with which some type of reflex from the carotid sinus occurs at the time of carotid ligations is not impressive. In most normal individuals it is difficult or impossible to induce such a reflex experimentally when the region is fully exposed at operation. It has been suggested (6, 30) that ligation of the internal carotid carries additional hazard because of resulting dilatation of the carotid sinus, subsequent fall in blood pressure, and therefore even greater embarrassment to cerebral oxygenation. Doubtless this possibility deserves some consideration, but the reflex can be avoided by infiltration of procaine into the carotid sinus and furthermore the dissection associated with placing a ligature about the internal carotid is usually sufficient to interrupt the important connecting nerves of the sinus. One should perhaps be equally on the alert for the reverse action, that of marked rise in pulse and blood pressure, sometimes attending ligation of the common carotid as in Case 3. Here the temporary relaxation of the arterial wall and of the intrasinal pressure is responsible for the reflex but it too can be avoided by the local infiltration of procaine, and by the time the effects of the drug have worn off there will have been sufficient compensation for the change in intravascular pressure.

That the ligations of the carotids in these patients materially lessened the arterial supply to the aneurysms is demonstrated by the diminution in the intensity of the bruit over the head and by the marked drop in the abnormally high oxygen content in the internal

jugular vein (see Cases 3, 4, and 5). The development in Case 4 of transient hemiparesis 2 days after the first carotid ligations and in Case 5 of 3 convulsions (her first) a few weeks after ligation was probably the result of thrombosis in some of the small vessels of the aneurysm. The generalized convulsions, coma, and death following the last ligation of the carotids in Case 4 were due to acute generalized cerebral anoxia rather than to any local effects upon the vessels of the lesion.

The benefit of simultaneous ligation of the proximal vein in arteriovenous aneurysms elsewhere in the body suggests that possibly simultaneous ligation of the internal jugular vein would be of comparable benefit (22). Its purpose would be to prevent the development of inadequate intravascular tension after carotid ligation. But since the arrangement of the vascularity of the brain is not quite comparable to that anywhere else, the indications for jugular venous ligation are not so clear.

Roentgenotherapy. One of the hoped for developments in a cerebral arteriovenous aneurysm is the eventual obliteration of the lesion by a process of gradual thrombosis. As a possible aid to this process the administration of x-ray radiation has justification. It was used to the limit in Case 3 and nearly so in Case 2, yet there is nothing to indicate that it produced the desired effects. It might be reasoned that the effectiveness of its use would be enhanced if ligation of the carotids had been performed first. Because of this it is planned to withhold roentgenotherapy in other cases, at least until after all has been accomplished with carotid arterial ligations that can be.

Cushing and Bailey were hopeful about the benefit of roentgenotherapy, principally from the developments in 1 patient. In this case re-exposure of the lesion after prolonged irradiation disclosed its almost complete devascularization and calcification.

Surgical attack of the cerebral lesion. This has not yet been tried on any of the cases of this series and there is little in theory or in others' experience with such attempts to recommend it. The most obvious argument against it, at least as far as the aneurysms involving the mid-cerebral artery are concerned, is that the blood supply to the motor cortex would most likely be destroyed if a radical excision or ligation of the proximal portion of the artery were attempted. Anything less than this, such as ligation of some of the vessels of the aneurysm, might serve to make the aneurysmal condition worse. Thus, the radical attack upon the lesions seems to be indicated only when hemorrhage threatens the patient's life.

In case the lesion should become inactivated by thrombosis of its vessels it might then be removed with greater safety. But if the indication for such a procedure should be convulsions alone, one should, as Dandy aptly points out, appreciate that there is no assurance of a permanent cure of epilepsy even after the cure of an aneurysm.

In an additional patient with a left cerebral arteriovenous aneurysm encountered since this paper was submitted for publication, a craniotomy was performed and the walls of many of the aneurysmal vessels on the surface of the brain were coagulated with the electrosurgical unit. The caliber of all the vessels treated in this manner was greatly diminished but few vessels became completely occluded. The procedure was followed by hemiparesis and aphasia from which there was slow but nearly complete recovery. The bruit was unaffected.

This method of treatment was suggested by Horrax[1] and deserves further trial in selected cases.

In résumé it may be said that the prognosis in individuals with cerebral arteriovenous aneurysms is not encouraging. All the methods of therapy discussed here leave much to be desired. But there is some merit in all of them, alone or in combination, and they can be used to advantage to suit the individual problem that each case presents.

SUMMARY AND CONCLUSIONS

1. Observations on 6 patients having cerebral arteriovenous aneurysms substantiate the conclusion that these lesions are congenital and can be identified both by the clinical signs and symptoms they produce and by their appearance when exposed at the operating table.

[1]Horrax, G. A two to eight year follow up study of 218 cases of benign brain tumor with special reference to the uncommon varieties. Tra. Am. Neurol. Ass., 1941.

2. A bruit heard on auscultation over some part of the head, the eyeballs, and the carotid arteries in the neck, is a characteristic sign. This, in conjunction with Jacksonian convulsions or unilateral motor and sensory disturbances, is usually sufficient to permit a diagnosis to be made.

3. Changes in the skull that may be shown on roentgenogram include slight signs of increased intracranial pressure; increased vascularity of the skull; deepening of the grooves for the middle meningeal arteries; local atrophy of the inner table from direct pressure of the vessels of the aneurysm; enlargement of the head; and calcification in the lesion.

4. Air studies may be relied upon, in many instances, to demonstrate abnormalities in the ventricles and subarachnoid spaces. Encephalography in such cases is safer than ventriculography.

5. Cerebral angiography is indicated in order to visualize the extent and the location of the lesion.

6. The collateral circulation is extensive. It involves anastomosis between the external and internal carotid arterial systems, principally through the orbit and through the meninges.

7. The effects of the aneurysm upon the general cardiovascular system are variable but not necessarily serious.

8. Headache, localized on the side of the lesion, is usually due to pain arising in the dilated arteries, chiefly in branches of the external carotid artery.

9. Reasonably safe methods of treatment include: exploratory osteoplastic operation and decompression, successive ligation of the carotid arteries in the neck, roentgenotherapy. None can be relied upon to be curative but used alone or in combination they may be beneficial.

10. Ligation of carotid arteries is safer in individuals with cerebral arteriovenous aneurysms than in others because of the rich collateral circulation.

11. Direct operative attack upon the lesions is dangerous but might be indicated in selected cases.

REFERENCES

1. Brock, S., and Dyke, C. G. Bull. Neurol. Inst. New York, 1932, 2: 247–293.
2. Cushing, H. Intracranial Tumors. Baltimore, Md.: C. C. Thomas, 1932.
3. Cushing, H., and Bailey, P. Tumors Arising from the Blood Vessels of the Brain. Baltimore, Md.: C. C. Thomas, 1928.
4. Dandy, W. E. Arch. Surg., 1928, 17: 190–243.
5. Deetz, E. Arch. f. path. Anat., 1902, 168: 341–352.
6. Dorrance, G. M. Ann. Surg., 1934, 99: 721–742.
7. Elkin, D. C. Ann. Surg., 1924, 80: 332–340.
8. Ferris, E. B., Jr., Capps, R. B., and Weiss, S. Arch. Neurol. & Psychiat., 1937, 37: 365–384.
9. Graham, J. R., and Wolff, H. G. Research Nerv. & Ment. Dis., Proc. (1937), 1938, 18: 638–669. Also Arch. Neurol. & Psychiat., 1938, 39: 737–763.
10. Gross, Sydney W. Proc. Soc. Exper. Biol. & Med., 1939, 42: 258–259.
11. Hawk, P. B., Bergheim, O., Oser, B. L., and Cole, A. G. Practical Physiological Chemistry. P. 407. Philadelphia: P. Blakiston's Son & Co. Inc., 1937.
12. Holman, E. Arch. Surg., 1924, 9: 856–879.
13. Idem. Arteriovenous Aneurysm; Abnormal Communications between the Arterial and Venous Circulation. New York: Macmillan Co., 1937.
14. Homans, J. Ann. Surg., 1920, 71: 707–718.
15. Hyland, H. H., and Douglas, R. P. Arch. Neurol. & Psychiat., 1938, 40: 1220–1232.
16. Keegan, J. J. Surg., Gynec. & Obst., 1933, 57: 368–379.
17. Leunenschloss, O. Cited by Cushing and Bailey. Loc. cit. (3).
18. Lindblom, K. Acta Radiol., Supplement, 1936, 30: 58.
19. Matas, R. In discussion on Dandy, W. E. Tr. Am. Surg. Ass., 1935, 53: 432–436.
20. Ray, B. S., and Wolff, H. G. Arch. Surg., 1940, 41: 813–856.
21. Reeves, D. L., and Stuck, R. M. Medicine, 1938, 17: 37–73.
22. Reid, M. R., and Andrus, W. DeW. Surgery of the Arteries. Nelson's Loose Leaf Surgery. Vol. 1. New York: Thomas Nelson & Sons, 1928.
23. Reid, M. R., and McGuire, J. Ann. Surg., 1938, 108: 643–693.
24. Rienhoff, W. F. Bull. Johns Hopkins Hosp., 1924, 35: 271–284.
25. Rotgans, J., and Winkler, C. Cited by Cushing and Bailey. Loc. cit. (3).
26. Schumacher, G. A., Ray, B. S., and Wolff, H. G. Arch. Neurol. & Psychiat., 1940, 44: 701–717.
27. Singleton, A. O. Ann. Surg., 1939, 110: 525–543.
28. Stertzing, P. Zentralbl. f. allg. Path. u. path. Anat., 1908, 19: 278–283.
29. Steinheil, S. O. Cited by Dandy. Loc. cit.
30. Sugar, H. S., and Meyer, S. J. Arch. Ophth., 1940, 23: 1288–1321.
31. Watson, W. L., and Silverstone, S. M. Ann. Surg., 1939, 109: 1–27.
32. Wolff, H. G. Research Nerv. & Ment. Dis., Proc. (1937), 1938, 18: 29–68.
33. Yater, W. M., Otell, L. S., and Hussey, H. H. Radiology, 1936, 27: 391–409.
34. Znojemsky, J. Cited by Dandy. Loc. cit.

THE SURGICAL TREATMENT OF ACUTE CHOLECYSTITIS IN PATIENTS FIFTY YEARS OF AGE AND OVER

FRANK GLENN, M.D., F.A.C.S., New York, New York

A NOTABLE advance in surgery in recent decades has been its application to patients of advanced years, for, at the beginning of the century, such patients were subjected to surgery only as a last resort. The medical literature today is granting an increased consideration to the question of lessening the risk of operation in patients over 50 years of age, for it is recognized that they form a large group, urgently needing surgery but accounting for many of its failures. The more intelligent preoperative treatment, safer anesthesia, and greater attention to operative details have removed many of the hazards of operation in older patients. In the surgical treatment of acute cholecystitis there persist two problems: one is the change in the biliary tract, the result of prolonged infection; the other, the systemic disorders common in advanced age. Acute cholecystitis in a patient over 50 years of age rarely is a simple acute inflammation in a formerly healthy gall bladder but is an exacerbation of a long standing chronic disease which may have damaged the entire biliary tract. The general systemic disturbances are vascular, such as arteriosclerosis, nephrosclerosis, cardiac disease, and hypertension. There is evidence for believing that there is an interaction between these conditions, or at least an unfavorable reaction of the organisms as a whole to long standing biliary disease, for the incidence of organic disorders, in our experience, is higher in patients with, than in those without, disease of the gall bladder. The patient 50 years of age or more who is admitted for surgical treatment of acute cholecystitis is, therefore, likely to be one whose biliary tract has been damaged and whose general systemic status shows signs of age beyond his years. For these, it is imperative that every precaution be taken to avoid complications following surgery. This obligates the surgeon to evaluate the risk in the individual case by every possible means and to combat, before operation, the manifestations of general systemic disturbances.

From the Department of Surgery of the New York Hospital and Cornell University Medical College.

Over a period of 7 years at the New York Hospital we have treated surgically 1,102 patients with nonmalignant disease of the biliary tract. In this group there were 267 patients suffering from acute cholecystitis and 835 with chronic biliary tract disease. The total number of patients 50 years of age and over was 276. There were 93 patients 50 years of age and over who had acute cholecystitis. It is with these patients that we are herein concerned.

The eldest patient was 75, and the average age for the 93 was 56.6 years. There were 64 women and 29 men. In seeking to estimate the duration of symptoms one is impressed with the difficulty with which adequate histories are obtained. If one is persistent the history is readily extended into the early decades. Intolerance to fatty foods, indigestion, belching accompanied at intervals with pain, nausea and vomiting, rarely accompanied by jaundice, constituted the frequent history. From a few patients a history of frank biliary tract disease of 30 to 40 years' duration was obtained. While it is true that some of the patients were too ill to permit the obtaining of a satisfactory history, it is highly improbable that the primary disease was of recent origin in any instance. The duration of the attack resulting in the hospitalization of the patient varied from a few hours to 10 days with an average time interval of 18 to 24 hours. That stones were present in the gall bladder or biliary passages of each of the 93 patients is additional evidence in favor of a process of long standing. In a review of over 1,100 patients with biliary tract disease we have found that the most complete histories place the onset of symptoms in women in the

twenties and early thirties, very often associated with the first or second pregnancy. In nulliparous women and in men it seemingly is about a decade later. The common dictum that gall-bladder disease is limited to the "fair, fat and forty" is only a partial truth.

In these patients 50 years of age and over, the surgeon is concerned not only with the biliary tract disease but with general systemic disorders as well. The incidence of systemic disturbance before operation was as follows: hypertension (diastolic over 90), 42 cases, or 45 per cent; arteriosclerosis, 47 cases, 50 per cent; cardiac disease, 38 cases, 40 per cent; diabetes, 10 cases, 10 per cent; renal disease, 8 cases, 8 per cent. By the term hypertension we refer to a diastolic pressure of 90 and over. Cardiac disease was indicated by cardiac enlargement as shown by roentgenograms, or coronary disease as evidenced by electrocardiographic changes. The diagnosis of diabetes was based on glycosuria and an elevated blood sugar. The diabetes was, for the most part, of a mild nature requiring only diet regulation after recovery from the acute illness. Two, however, were severe enough to require fairly large dosages of insulin. Impaired kidney function as determined by urine concentration, urea clearance, and the persistence of an albuminuria following recovery from the acute illness was found in 8 patients. It has been our experience that albuminuria, elevated urea nitrogen, and the presence of blood cells in the urine during the acute illness often disappear as the patient's condition improves. The occurrences of these disturbances is of much higher incidence than in a similar age group without biliary tract disease.

OPERATIVE PROCEDURES

The procedure of cholecystostomy was performed in 16 instances. Four deaths followed. This operation is clearly indicated under certain circumstances; as when the patient is too ill to withstand cholecystectomy, or when cholecystectomy presents too great difficulties. For the extremely debilitated patient or for the very ill, we doubt if there are any contraindications for cholecystostomy because it may be done under local anesthesia, disturbing the patient very little. Such an operation may be a lifesaving procedure. It decompresses the biliary tract and averts catastrophe by preventing progressive liver damage if complete biliary obstruction is present. In this group of 16 patients who were treated by cholecystostomy it appears to us that the conservative procedure was responsible for the recovery of the very ill patients. The 4 who died were in such straits that it is very likely that they would have died regardless of whether or not they were operated upon, and furthermore, regardless of the type of operation. Five of these patients later had cholecystectomy performed. Four were uncomplicated; 1 at operation was found to have a fistula between the lower portion of the gall bladder and the duodenum. All made an uneventful recovery.

Cholecystectomy was carried out in 69 patients with 2 deaths. This, when feasible in the opinion of the surgeon, is the operation of choice because it removes the primary site of the disease as well as the principle source of acute complications. Generally speaking, the acutely inflamed gall bladder is removed with ease. However, in this group of patients cholecystectomy may be difficult. It should be done with care, subjecting the liver to a minimal amount of trauma.

Common duct exploration in acute cholecystitis has been limited by us to the same indications as in chronic biliary tract disease. If it is indicated the duct should be explored and stones removed. The incidence of postoperative complications was not apparently increased by this procedure in this series. Twelve patients were subjected to common duct exploration—stones were present in 6, or 50 per cent. It would seem that the urgency of the situation when a stone is in the common duct outweighs the hazards of the procedure. Decompression, i.e., cholecystostomy, may be utilized as a compromise procedure, the plan being to explore the common duct at a later date when the patient's condition has improved. In this group of patients only 1 such case was encountered.

At operation there were found 64 instances of acute cholecystitis, 18 instances of acute cholecystitis with gangrene, and 11 instances of acute cholecystitis with gangrene and per-

TABLE I.—SUMMARY OF DEATHS AFTER OPERATION

	History number	Sex	Age	History of biliary disease	Duration of attack	Jaundice	Findings	Operation	Cause of death
1.	51,896	F	66	8+ yrs.	3 days	+	Acute cholecystitis with perforation. Peritonitis	Cholecystostomy, drainage	Peritonitis
2.	155,437	F	67	4+ yrs.	7 days	0	Acute cholecystitis with gangrene	Cholecystostomy	Peritonitis, bacteriemia
3.	221,902	F	50	20+ yrs.	10 days	+	Acute cholecystitis, cholelithiasis, common duct obstruction	Cholecystostomy	Bacteriemia, stone in the common duct, thrombosis of hepatic artery
4.	182,841	M	72	7+ yrs.	8 days	+	Acute cholecystitis, cholelithiasis	Cholecystostomy	Liver failure, biliary cirrhosis
5.	134,502	F	57	inadequate history	4 days	0	Acute cholecystitis, cholelithiasis	Cholecystectomy, drainage of abscess	?Subheptaic abscess *
6.	59,204	F	70	12+ yrs.	8 hours	0	Acute cholecystitis, cholelithiasis	Cholecystectomy	Coronary occlusion, cardiac failure

*No Autopsy.

foration. In determining the type of operation to be done, the gross appearance of the presenting pathological changes is of importance. In the first place, if there is gangrene and perforation with an accompanying generalized peritonitis, we recommend simple drainage of the abdomen together with cholecystostomy. If there is gangrene and perforation which has resulted in a localized peritonitis or abscess in the region of the extrahepatic portion of the gall bladder, then one may choose between cholecystectomy and cholecystostomy. However, in the presence of extensive adhesions of the omentum to the gall bladder and into the biliary fossa it is indeed questionable whether these should be disturbed and a cholecystectomy done. If the patient is unusually ill and if postoperative complications appear in the offing, then certainly cholecystectomy should not be attempted. Perforation of the gall bladder with a small abscess or perforation into adjacent liver tissue is no contraindication to cholecystectomy. The patients with simple acute cholecystitis are, in general, best treated by cholecystectomy.

In the summary of this series of patients who were treated surgically for acute cholecystitis the following facts emerge: first, biliary tract disease had been present for many years, and second, vascular changes commonly associated with age occurred far more frequently than in a comparable group without biliary tract disease. As to the first, we were concerned about the duration of the biliary tract disease since its beginning as well as with the present acute episode. Frequently the attack which brought the patient to the hospital differed from many previous attacks only in severity and failure to subside. The significance of this failure to subside is seen in the deaths; 4 of the 6 had been acutely ill for 4 to 10 days (Table I).

A careful investigation and evaluation of each system was made in these patients. The most frequent finding was dehydration and we believe a depletion of chlorides and glucose. Parenteral glucose and saline readily correct these deficiencies. Cardiac failure, when present, impending, or anticipated, has been combatted by immediate and rapid digitalization without cause for regret so far. Sometimes cardiac and biliary symptoms are indistinguishable in these patients. Support to the cardiac mechanism in doubtful cases is not withheld.

The presence of jaundice requires determinations of blood prothrombin and the bleeding tendency, and may indicate blood transfusions, bile salts, and vitamin K. Sulfonamide drugs should be given if a bacteriemia is discovered.

Anesthesia. The selection of anesthesia depends on the condition of the patient and requires judgment because many postoperative complications are attributed to it. 'Local anesthesia may often be used to advantage for limited procedures such as cholecystos-

tomy and also for the beginning of an operation, general anesthesia being substituted if a greater procedure is decided upon. Our experience thus far leads us to believe that open drop ether is the safest general anesthesia for these patients. First of all, it is satisfactory from the standpoint of relaxation allowing an adequate exposure and aiding thereby to the ease with which the operation can be done; and, secondly, in our hands, the incidence of postoperative pulmonary complications is less than in those patients who had other types of anesthesia.

The distribution of anesthesia in the series was as follows: local in 12 patients; spinal in 2; ether in 32; ether in combination in 10; ethylene in 19; cyclopropane in 18.

Postoperative complications. These are grouped for convenience into pulmonary, cardiac, wound, and miscellaneous complications.

There were 4 pneumonias, 2 of which were bronchopneumonias, 1 following local anesthesia, 1 following cyclopropane. Lobar pneumonia occurred in 2 patients after open drop ether anesthesia. All recovered without residual complications. Pulmonary infarction occurred twice, one associated with a phlebitis of the leg. Two patients had atelectasis of the right lower lobe which was discovered early and cleared without prolonging the patients' hospital stay; both of these were following open drop ether anesthesia. These patients ranged in age from 50 to 65. The incidence of postoperative pulmonary complications is only slightly higher than for patients under 50 years of age.

Pulmonary edema followed auricular fibrillation in 1 instance, but the patient recovered after digitalization. Auricular fibrillation was not considered a postoperative complication unless accompanied by some manifestation of cardiac failure. In 3 patients there occurred cardiac failure sufficient to produce dependent edema which cleared as the patients' condition improved or as digitalization was completed.

There were 2 instances of wound dehiscence. In one there was gross infection of the wound, in the other cultures taken were negative for bacterial growth. It was ascribed to postoperative hiccoughing and vomiting. The wounds were resutured with through-and-through silver wire. Four wounds were superficially infected and 3 showed infection extending down to and involving the fascia. There were 2 hematomas, one occurring in a jaundiced patient and another in a non-jaundiced patient who had cirrhosis of the liver.

Two patients following operation were found to have a positive blood culture, 1 due to colon bacilli and 1 due to Bacillus lactis aerogenes. The same organism was obtained from the peritoneal cavity at the time of operation and blood cultures became negative as the clinical condition improved. Three patients developed phlebitis of the lower extremities without accompanying pulmonary emboli.

The average age of the 6 patients who died was 63.6 years. All but 1 were found to have had unmistakable symptoms of gall-bladder disease for years. The duration of the attacks, with 1 exception, was prolonged over a period of days before admission to the hospital. Jaundice was present in 3 of the 6 patients. The findings at operation included those complications which take place in acute cholecystitis, namely, gangrene with perforation, abscess formation, peritonitis, common duct obstruction, and bacteriemia. There was only 1 instance of uncomplicated acute cholecystitis in the 6 deaths, and death in this patient was due to coronary occlusion.

The expectancy of life at birth has been almost doubled during the past half century in the United States (3). Our general population is, therefore, becoming one with a greater percentage over 50 years of age. The surgical therapy accorded these people is on the increase. And although malignant disease is the most common ailment requiring surgery in the later decades, biliary tract disease is by no means rare, as is evidenced by the foregoing résumé. Surgery in the early phases of biliary tract disease should be looked upon not only as an immediate therapeutic measure but also as a preventive one. We have observed in our own series of cases that the mortality in the treatment of gall-bladder disease increases with the age of the patient. In 826 patients under 50 years of age the post-

operative mortality was 1.0 per cent; in 186 patients from 50 to 59 years of age was 7.5 per cent; in 77 patients from 60 to 69 years of age was 13 per cent; in 13 patients of 70 or more years, 30 per cent. For 93 patients with acute cholecystitis, 50 years of age and over, the mortality was 6.4 per cent.

The data collected in our experience suggest that the changes in the vascular system, i.e., arteriosclerosis, hypertension, etc., are greater in these 93 patients than in a corresponding number without biliary tract disease. Cowdry (1) in a volume on arteriosclerosis places the incidence of arteriosclerosis in the general population at 25.6 per cent for those between 50 and 60, and 38 per cent for those over 60. McCallum (2) found that patients over 50, dying as a result of gall-stone disease in the Johns Hopkins Hospital, showed an incidence of arteriosclerosis in 68 per cent.

The surgical treatment of biliary disease and its complications makes up only a part of the surgery of geriatrics. This small series of 93 patients with acute cholecystitis represents rather well a common problem today. They should be regarded with great care. Preventive surgery should reduce their number, i.e., the surgical treatment of biliary tract disease in the earlier decades when acute cholecystitis represents an early phase of the disease. If our contention is correct, a deleterious effect upon the vascular system may be interrupted.

CONCLUSIONS

1. Acute cholecystitis occurs frequently enough in patients over 50 years of age to warrant special consideration by physician and surgeon.

2. In this group of patients acute cholecystitis may well be looked upon as a complication of a disease of long standing.

3. The incidence of organic disorders, and in particular those of the vascular system, is higher in patients with, than in those without, biliary tract disease.

4. Acute cholecystitis in patients over 50 years of age requires urgent surgical consideration.

5. The trend of our population toward the older age groups indicates that we may anticipate an increasing number of these geriatrical problems in the practice of surgery.

6. The recognition of the extent of the clinical problem involved in the care of these patients, the employment of adequate but conservative surgical therapy, and the according of proper attention to the vascular system should contribute to a further reduction of the mortality rate.

REFERENCES

1. Cowdry, Edmund V. Arteriosclerosis. P. 361. New York: Macmillan Co., 1935.
2. MacCallum, W. G. In Cowdry's Arteriosclerosis. P. 359. New York: Macmillan Co., 1935.
3. Medical practice and our aging population. Statistical Bull., Metropolitan Life Ins. Co. 1941, 22: No. 4–1–3.

CONGENITAL CLEFTS OF THE FACE AND JAWS

A Report of the Operations Used and a Discussion of the Results

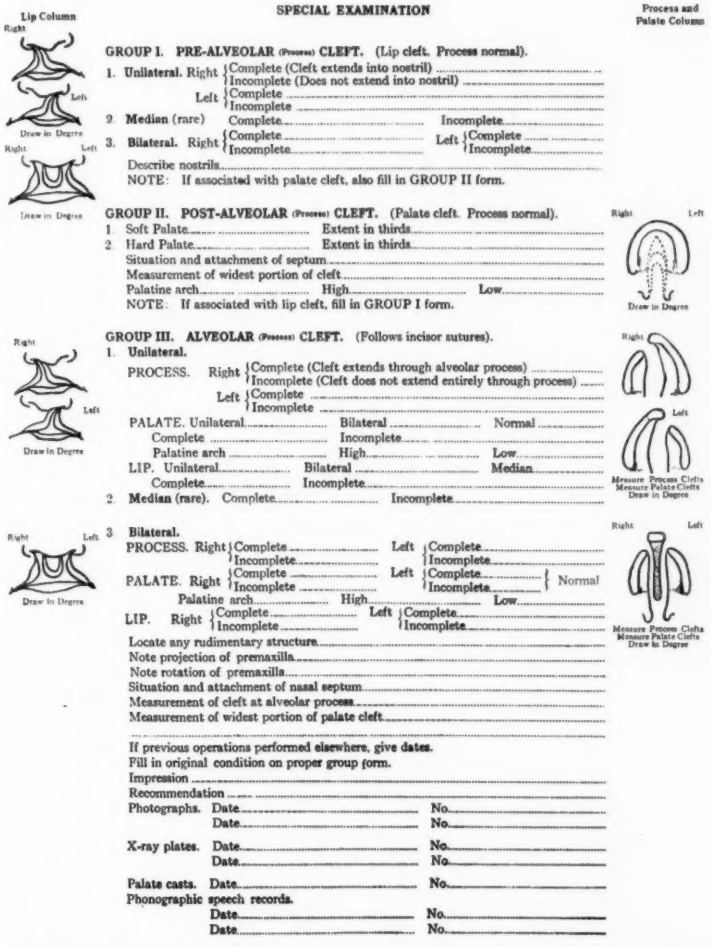
HARRY P. RITCHIE, M.D., F.A.C.S., St. Paul, Minnesota

IN a chapter bearing the same title as this article (5), the writer has detailed a voyage of discovery made through many channels of interest in an urgent effort to find an answer to the question "What should be done?" to reconstruct the deformity and prepare the baby for future growth and development. Based on the findings in the embryology, anatomy, and physiology of the tissue involved, some suggestions were made on the technical steps of operations, and the reasons for them were stated. The steps of procedure were illustrated by diagrams. In 1936, I had an opportunity of revising the chapter, in order to withdraw statements and illustrations made on the use of direct force applied to the upper jaw, which I did because of my experience in the use of wire and plates. Such distressing results followed their use, with malocclusion and long years of orthodontia, that in some cases the surgical deformity seemed worse than the embryonal deformity, so I could not allow the plans to remain permanently in the literature. Since that revision, and particularly since the first printing, many notable papers have appeared in the literature suggesting new plans, and modifications of combinations of old ones, offered by men of wide experience, so many that I felt that they should be discussed in relation to the propositions made in the chapter. Most of the more recent papers have to do with the palate. The dental surgeons are also entering the list of contributors, to indicate that what we have been doing to the hard palate interferes with the normal development of the upper jaw. This is a most important observation, because it is the late results which are the most important, and it is up to us who do the primary repair to take cognizance of these reports.

I thought that, instead of merely discussing these new plans, I would show a series of cases, tell what was done to them, locate the newer suggestions, discuss more fully the age for, and sequence of, operation and frankly criticize the results of my operative efforts. The cases are shown in the order of the classification and plan of record, the whole story of the development of which has been covered in my contribution to *Practice of Surgery* (5).

GROUP I. PREALVEOLAR PROCESS CLEFT. THE GROUP I CASES

Dr. Sherman's descriptive term is used for those cases in which the deformity is in front of a normal process and therefore is one of a lip problem only. Four cases are here shown to illustrate common degrees, with the caution that really no 2 cases may be exactly alike, and that in between these 4 cases there are those which merge from one degree into another. This deformity has been described as a simple harelip. The term "incomplete harelip" is also applied because there is never a cleft in the floor of the nostril, although, as in Figure 4, the ala may show some distortion. These cases, however, constitute a most important group, because the lip cleft is the only cleft present and thus can be subjected to the closest study. It was the clinical observation of these cases which led to the anatomical and physiological study of the tissues involved, which in turn led to the conclusion that the various forms and degrees of any cleft lip were readily explained by the position and disposition of the muscle elements in each case. The muscle theory repair of the lip was presented in 1928 and has been elaborated in the chapter in *Practice of Surgery*. It was an effort on my part to find some index to lead me to a proper repair of the lip which would substitute any personal opinion as to how it should be done, and would be something that would fit any lip. Review these cases carefully, as I believe that the conclusions are obvious and are fundamental to repair of any lip cleft.



Lip Column

SPECIAL EXAMINATION

Process and Palate Column

Right

Left

Draw in Degree

GROUP I. PRE-ALVEOLAR (Process) CLEFT. (Lip cleft. Process normal).

1. Unilateral. Right {Complete (Cleft extends into nostril) / Incomplete (Does not extend into nostril)
Left {Complete / Incomplete
2. Median (rare) Complete Incomplete
3. Bilateral. Right {Complete / Incomplete Left {Complete / Incomplete
Describe nostrils
NOTE: If associated with palate cleft, also fill in GROUP II form.

GROUP II. POST-ALVEOLAR (Process) CLEFT. (Palate cleft. Process normal).

1. Soft Palate Extent in thirds
2. Hard Palate Extent in thirds
Situation and attachment of septum
Measurement of widest portion of cleft
Palatine arch High Low
NOTE: If associated with lip cleft, fill in GROUP I form.

Draw in Degree

GROUP III. ALVEOLAR (Process) CLEFT. (Follows incisor sutures).

1. Unilateral.
PROCESS. Right {Complete (Cleft extends through alveolar process) / Incomplete (Cleft does not extend entirely through process)
Left {Complete / Incomplete
PALATE. Unilateral Bilateral Normal
Complete Incomplete
Palatine arch High Low
LIP. Unilateral Bilateral Median
Complete Incomplete
2. Median (rare). Complete Incomplete

Measure Process Clefts
Measure Palate Clefts
Draw in Degree

3. Bilateral.
PROCESS. Right {Complete / Incomplete Left {Complete / Incomplete
PALATE. Right {Complete / Incomplete Left {Complete / Incomplete } Normal
Palatine arch High Low
LIP. Right {Complete / Incomplete Left {Complete / Incomplete
Locate any rudimentary structure
Note projection of premaxilla
Note rotation of premaxilla
Situation and attachment of nasal septum
Measurement of cleft at alveolar process
Measurement of widest portion of palate cleft

If previous operations performed elsewhere, give dates.
Fill in original condition on proper group form.
Impression
Recommendation
Photographs. Date No.
Date No.
X-ray plates. Date No.
Date No.
Palate casts. Date No.
Phonographic speech records.
Date No.
Date No.

Measure Process Clefts
Measure Palate Clefts
Draw in Degree

Fig. 1. The reverse side of the record chart is reprinted for the convenience of the reader who may not be familiar with the terms of the description of the cases which are recorded, not as harelip and palate cases but as a series of congenital clefts of the face and jaws. The clefts are grouped on the alveolar process as to the position of the clefts in relation to a normal or a cleft alveolar process, thus developing a name for the case as a whole, to indicate the position and combination of the clefts present in that case. The arrangement of the diagrams and literal translation between them was made by Dr. John Staige Davis. In 16 years of use but one change from the original has been made. In the "Group III, Alveolar (process) Cleft" cases, in both the unilateral and bilateral combination, about 10 to 12 per cent of the cases have a normal hard and soft palate, so the word "normal" has been inserted in the palate description.

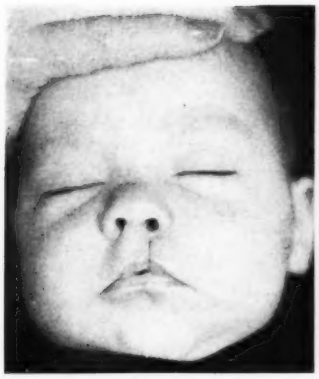


Fig. 2a.

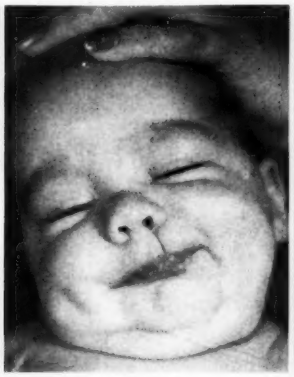


Fig. 2b.

Fig. 2c.

Fig. 3a.

Fig. 3b.

Fig. 2. a, The case with a mere marking of the lip is usually advised against operation, as that case presents a minimal cosmetic deformity with no dysfunction. But when the line is depressed or becomes increased in depth on motion, the deformity should be corrected, because if the explanation of the defect is accepted, there is every expectation that the deformity will increase in degree on growth of the child. With the embryology, anatomy, and physiology of the lip tissues in mind, it can fairly be said that in this case the condition is due to the fact that the superficial strata of the muscle bundles in the body of the lip have failed to complete their migration and thus do not interdigitate with their fellows on the opposite side, but instead are attached to the skin and when contraction occurs the line is depressed. Of course, it is not surgically possible to identify the muscle elements, but they can at least be apposed in the line or curve of their action. Freehand incisions made on each side of the skin cleft and removal of the skin involved exposes the body of the lip. Interrupted stitches are inserted on one side at a time, deep enough to include the exposed body. If the exposed bundles are found to be contracted under the skin, they are defined by gentle undercutting of the skin sufficiently to include them in the stitch and are pulled out with a hook to insure their inclusion in the bite of the stitch. Such a procedure offends a fundamental principle in wound suture, viz., layer series suture of the tissues, but it is done here because I believe buried sutures in the body of the lip should not be used. This opinion may be modified in the future, because there are several materials now being presented as nonirritating, but I can state from experience that buried catgut may be a cause of later trouble. This case is offered as a model for the repair of any lip, as it illustrates the normal formation of the lip, and all I did was to complete the job by a simple surgical procedure. Great care must be taken in the exact placing of the stitch at the mucocutaneous vermilion border (see Case 2). b, Shows a voluntary contraction, outlining clearly the musculature of the lip, and points of denudation are definitely made. Please note the V-shaped depression in the lip at the base of the nostril. The same picture can be obtained by electrical stimulation while the baby is asleep. c, Please note the line of the vermilion border, the oblique direction of the suture line, the eversion of the lip, which is quite similar to the lower lip.

Fig. 3. Group I. Prealveolar process cleft. Right incomplete.

In this case there is no marking on the lip except a notch at the vermilion border, which means that the superficial strata of the orbicularis oris have interdigitated, but the bundles in the body of the lip and under the mucous membrane are apart, causing a thin lip at this point without much cosmetic deformity, but with definite dysfunction of the lip. The ends of the bundles can be denuded from the mucous membrane side but the approach and suture are awkward. It requires a bit of surgical courage to break the lip down and pay the penalty of a skin scar, but since precision is a prime principle, this was done. When the body of the lip is thus denuded it is possible to put the muscle stitches in from the mucous membrane side and thus exclude possible stitch marks. By so doing the deep stitches can be removed and this excludes any worry about buried stitches. This case illustrates the care necessary in suturing the vermilion border. Note the outlines of the prolabium of the embryonal frontonasal process in photograph at left and its postoperative aspect in photograph at right.

Fig. 4. Group I. Prealveolar process cleft. Left incomplete. a, The description of this case must be written in on the chart, to describe the fact that the cleft is incomplete above and complete in the lower two-thirds, and a drawing made on the diagram. While cases as in Figures 2 and 3 are not so common, this degree is most frequent. It is not my intention to repeat aforementioned studies and conclusions, but in looking at this picture, the temptation to analyze the conditions here present is too great to resist. In the lower two-thirds of the left side of the lip, the skin, body, and mucous membrane are entirely apart. In the upper third the skin and mucous membrane have contacted, but the body of the lip is thinner than normal, a condition similar to that in Figure 2. The nostril is flatter than that on the right side. The aspect of the right nostril and right side of

Fig. 4a.

Fig. 4b.

the lip is that of a normal lip. This is explained by the fact that the muscle elements on the right side have migrated from their origin in the platysma, up the soft tissues of the right maxillary embryonal process, proceeded through the prolabium of the frontonasal process and appear at the cleft margin in position to interdigitate with the fellows of the maxillary process which is out of contact. The outlines of the skin of the prolabium, which, of course, has a different origin from that of the sides, can readily be made out, with a normal vermilion border on the right, while at the cleft margin it is indicated by an obtuse angle. The tissue on each side of the cleft appears equal in length and bulk, and the obvious thing to do is to denude the bodies of the lip and sew them together as they lie, the same problem as in Figure 1. b, There is a margin of personal interpretation of the result of electrical stimulation. On the combination side it is constantly evident. On the side out of contact the bundles often appear bunched and the lower point of contracture not so definite, particularly if the tissues have been handled and because the immature muscle bundles tire quickly. When uncertain the tendency is to ink a mark too close to the cleft, and an angle appears in the vermilion border, as in this case. The angle is entirely superficial, but a result of more severe degree may give still a picture of cleft lip at this point. On the contrary, if the denudation is made too far out and the muscle stitches not precisely and symmetrically placed, the side out of contact is displaced downward and a staggered lip repair is obtained. Such results are purely technical failures and have nothing to do with surgical principles of the cleft lip operation, because in

Fig. 5a.

Fig. 5b.

this case it is evident that the body of the lip has healed, and the right and left facial expression groups have been co-ordinated.

Fig. 5. Group I. Prealveolar process cleft. Left incomplete. a, This degree has been described as incomplete—a simple harelip—but with the muscle theory in mind it is a complete cleft, as there is no muscle contact anywhere along the line. This form of lip cleft is historically interesting, because it is the model upon which are drawn the lines of incision of the original Mirault operation. When I was groping around, trying to follow set operations, I noted that, with this operation, the best looking nostrils were obtained, and I never knew why, but the reason now is readily explained by the fact that the curved sweep of the upper part of the incision would denude the upper bundles of the orbicularis oris, remove the overlying epithelial tissue, and thus accomplish empirically what I have gone to such lengths to prove is a necessary step in the repair of the deformity. The technical steps in the repair of this lip are briefly repeated: The demonstration of the position of the active tissue, symmetrical denudation and suture side to side as in Figure 1, taking cognizance of the principle of layer series suture by placing the deep stitches from the mucous membrane side to include the muscle bundles and out fold the mucous membrane, which, with interrupted stitches in the skin, sutures three kinds of tissue with only two forms of stitch and thus meets the fundamental principle in wound repair. b, The only difference between this lip and the complicated picture of the group III lip is in the matter of degree, due to conditions outside of the lip itself.

GROUP II. POSTALVEOLAR PROCESS CLEFT

THE GROUP II CASES

This is Dr. Sherman's term of description for the case in which the deformity is behind a normal process. The incidence is somewhat confused, because this condition may come in for correction at any time of life, whereas in the group I and group III cases, the deformity is readily apparent, and advice is sought at, or soon after, birth. Approximately one case in five can be accepted as almost right. This case has been described as an incomplete or simple cleft palate, because the alveolar process is normally formed, but it is a cleft palate case. A great part of the literature is composed of discussion of the relative merits of various technical procedures called cleft palate operations, which are, it seems to me, presented without regard to the form, degree, or association with other clefts which may be present in the case.

The group II cleft palate has been brought into the limelight in the past few years by Dr. George Dorrance of Philadelphia, who offered the push back operation, which was based on the belief that postoperative speech defect was due to a short palate, and that this defect could be overcome by raising the hard palate tissues in the form of a delayed flap, at one sitting, and then later attaching the forward margin of the mucoperiosteal flap to the hori-

Fig. 6a.

Fig. 6b.

Fig. 6. Group II. Postalveolar process cleft. Soft palate only. a, There is no formal diagram for this degree and the description must be written and drawn in. The condition appears only occasionally and is usually overlooked or considered so minimal that no particular attention is paid until the patient develops a speech defect. The apparent deformity is that of a uvula cleft which in itself is of no consequence, but the presence of a cleft uvula may be and usually is an index that the muscle bodies of the soft palate are apart in various degrees, up to complete failure of contact, causing a transparent soft palate, the so called submucous cleft palate. It requires some courage to break the palate down, find the muscles, and make a formal repair. This was done and the postoperative improvement in speech in this case was remarked by the whole hospital. This condition in the soft palate is comparable to that in Fig. 3 a in the lip, i.e., failure of complete muscle contact. b, The superficial stitches come out in the food and it is only necessary to remove the deep stitches about the fifth or sixth day. The soft palate at rest hangs down at an appreciable distance from the pharynx. The space can only be contracted by muscle action. The ability of this boy to speak depends upon the proper union of the two halves and whether the muscles of the soft palate are hooked up with the superior constrictor of the throat. If they are not united then he will have a curtain soft palate, without action or function.

zontal plate of the palate bone, thus bringing the soft palate into contact with the pharyngeal wall. Barrett Brown, of St. Louis, has followed up this procedure with several further technical suggestions. My difficulty has been in selecting the case and deciding to do the operation, for the reason that I have not accepted the plans as primary procedures, because over many years of observation I think I have obtained equal results by much simpler operations, paying particular attention to the severing of the soft palate from the bone and to the suture of the musculature of the soft palate. In discussing the cleft palate operations, I have selected four primary case conditions to show that, because the process is closed, there is always a picture of a median cleft, which clinically supports the embryological fact that the hard palate is formed from the sides, and that the median process which is so important in the process and the lip is not a part of the hard palate. All cases in this group have the same form of median cleft, with equal tissues on each side. One case differs from another in involvement anteroposteriorly, and this runs from a cleft in the uvula to the anterior palatine foramen. Look at Figures 6, 7, 8, 9, and 10. They are all median clefts. The obvious thing to do is to move the tissues to the midline and sew them together. The pioneers recognized this and there has come down to us an operation which is now classical, called the Langenbeck or Warren Langenbeck. This, of course, is simply a lateral sliding flap of the mucoperiosteum of the hard palate, mesially sutured, plus the median suture of the soft palate. Objections to the operation on the hard palate have long been recognized and these objections have been used in support of the many substitute operations which have been offered. Even Dr. Brophy used the sometimes necessary lateral incisions to the support of his compression methods applied to the upper jaw, although I have failed to see any suggestion of the compression methods being used in the group II cases.

Professor Veau, the master French surgeon, discussing the "division palatine," succinctly states his objections to be that the elevation and suture of the mucoperiosteal flaps leaves a blind space between the flap and the bone for the accumulation of blood clots and nasal discharge, with a chance of infection and scar formation, and that lateral incisions do not always heal and may heal by scar formation. This is an objection made by the dental surgeons, with which I heartily agree, but I wish to add one objection which is the most important of all. The classical Warren Langenbeck operation is just too much surgery to be done at one time. It was based on the whole palate theory and failed to recognize that it constituted two operations dealing with tissues entirely divorced in anatomical structure and function. Almost all of the operations deal with the hard palate, and there has been so little said about the soft palate. Professor Veau has recognized the importance of the tensor palati by his submucous wire placed to include it. Wardill has made a beautiful anatomical study to show the contact of this mus-

Fig. 7a. Fig. 7b. Fig. 7c. Fig. 7d.

Fig. 7. Group II, 1/3. This degree is most important, and I propose to relate in detail my experience in the care of this case, because so many points are brought up which are so often discussed in the literature: (1) The incidence is high. (2) I have found that in many cases the cleft in the bone is further forward than appears in the soft parts. (3) Over the cleft in the bone the tissue is no more than mucous membrane, so very thin and delicate that failure to recognize this fact may be followed by failure of union. (4) The surgeon has so many operations from which to choose that he may be confused—(a) the soft palate may be denuded as it lies, by removing a strip of mucous membrane and the bared muscles sutured; (b) follow the plan elaborated in the next case (Fig. 8); (c) follow the push-back operation of Dorrance in two sittings; (d) follow the plan of Barrett Brown, in one sitting. This girl was 5 years old, well within the age limit for the push back operation and the degree of the cleft meant that the greatest distance in backward displacement could be obtained. This operation was performed by elevating the hard palate flaps, rupturing the posterior palatine arteries and replacing the flap in its original bed. Following this, she developed a middle ear condition, which is no objection to the operation, as it may occur after an operation of any kind. She did not return for 2 years. At the age of 7, at which time picture b was taken, I found that the mucoperiosteal flaps were twice the thickness of the original state, that the blood supply was so luxuriant as to be a matter of concern during the operation. It was controlled in this case by infiltration of adrenalin, 3 drops to 1 ounce of saline. The flap was so thick that ordinary sutures would not hold it to the bone, so I perforated the palatine process with wire, anchored it over a Brophy lead plate and held it with perforated shot. Then the soft palate was done, i.e., I did two operations at one time. On the sixth day, picture c was taken to show all stitches holding. Two of the deep stitches were removed, but such was her resistance that the removal of the last stitch was postponed until the next day, at which time, with all the operations and treatment, the little girl was in a frenzy. But I persisted in the removal and simply tore the wound apart, as shown in d. Here is an illustration of a failure which was due to a mechanical separation of the wound, without loss of tissue and it is offered as a caution for care in the removal of stitches. In spite of the fact that the hole in the soft palate will be nearly closed by contraction, it will be necessary to break the palate down, find the muscle, and perform a formal repair, as depicted in Figure 6a and Figure 6b.

cle with the superior constrictor of the pharynx at the hamular process but most operations on the soft palate, as I interpret them, fail to recognize the fundamental principle in wound suture, i.e., series layer sutures. The soft palate is repaired in the same way that I used to see laparotomy wounds sutured, with the Peasley needle. Through-and-through stitches will contract any denuded surface. Robert Ivy, of Philadelphia, has recently quoted Axhausen in a procedure in which the pharyngeal mucous membrane of the soft palate is sutured, the muscle bodies united by buried catgut stitches and then the oral mucous membrane approximated separately, which is exactly right. I fear the buried muscle stitch and believe some tension stitch should be used, because as soon as the muscle bodies are united, contraction takes place and pull against the muscle stitches occurs. I favor removable stitches used in the form of a vertical mattress or of a figure of 8, i.e., the small and large bite stitches supplemented by single stitches in the mucous membrane, beginning on the oral side and carried around on the uvula to the nasal mucous membrane side, ending up at the posterior pillars. Precision is essential or one may get a postoperative result similar to the congenital condition shown in Figure 6a or a complete failure as in Figure 7b. To fill the dead space between the bone and the palate flap, Professor Veau has suggested the use of the mucous membrane of the vomer, which is used in the form of a flap dovetailed under the mucoperiosteum of the hard palate, thus filling the dead space. This flap so used closes up the nasal canal, but it does not close the cleft palate, to complete which it is necessary to suture

Fig. 8a.

Fig. 8b.

Fig. 8. Group II. Postalveolar process cleft, 2/3. The cleft in the horizontal plate and the palatine process is most evident. This is the easiest palate to do and with a minimum amount of traumatism. There is little to be gained by a push back. The mucoperiosteal flaps may be raised from the cleft margin. When this is done, the mucous membrane attachment of the soft palate to the horizontal plate of the palate bone is definitely demonstrated and easily severed, a necessary step and one I have used from the first palate operation I ever did. The ends of the tensor palati are positively identified and thus can be precisely sutured. The objection to denuding the soft palate by transfixation is that the tensor palati may or may not be evident. But contrary to the lip, in which no separate muscle bundles may be found, here there is an easily identified muscle, the suture and union of which are a crucial step in the repair. Should a failure of union take place there is still a cleft palate, and complete function cannot be expected. Lateral incisions may or may not be required, but they are usually used, because by so doing it seems to me that I accomplish to some degree at least the purposes of the more extensive push back. By far the most cases, by this simple procedure, obtain the aspect of a normal palate. This patient is now a beautiful girl of 16, who fully enters the social group of her age, has developed a fine singing voice, and who takes part in school operettas and platform speaking, so I believe that the steps of operation as outlined are primary procedures, and should a result be less satisfactory than in this case, recourse may be had with gratitude to the more extensive operation of the push back and its modifications. This girl has been recently checked up on speech according to the plan developed by Dr. Wallace Ritchie. This test was done in the presence of a group of the family and office members, with instruction for each one to indicate even the slightest divergence from the normal. There were no comments, with the conclusion that her speech was absolutely normal. To me she is the support of everything I have said about the reconstruction of the palate. b, The spot in the picture on the soft palate is not a hole, but mucous membrane humped up into a red spot. The uvula looks like the one in Figure 6a, but of course is only a technical defect, in that the halves are staggered or the stitches pulled out. This condition has absolutely no effect on her speech.

Fig. 9 a and b. Group II, 3/3. The cleft extends to the anterior palatine foramen. It still has the aspect of a median cleft. This case brings up several problems of age for operation and proper operative procedure. I saw this child soon after birth. She was a very delicate child, with a cleft so wide that it seemed impossible to close. She was placed in the hands of a pediatrician who gave her the most careful attention, but it was not until the child was nearly 3 years old that I obtained his permission to operate, and then only because of my promise that the hard palate operation would cause no shock. The hard palate was infiltrated with salt solution containing 3 drops of adrenalin, which does control bleeding temporarily. The mucoperiosteal flap was raised from the cleft margin and the space behind it, and the bone was packed with a section of dental roll. This may be an excess of precaution, but so often I see that loss of blood in any operation seems to be in direct ratio to postoperative concern. The mucous membrane attachment of the soft palate was severed. Lateral incisions were made and packed with benzoid dental cotton roll, in an effort to release tension on the hard palate stitches, but also to hold the soft palate in the backward position. Lateral mattress stitches were placed in the hard palate in order to bring the periosteum into contact. The interrupted stitches were placed in the mucous membrane. By so doing, the fact that the covering of the palatine processes is composed of two different kinds of tissue is recognized. Mere contact of the edges of the cleft by a continuous or interrupted transfixation stitch invites defeat. In 6 months the posterior part of the healed hard palate was elevated and the mucous membrane of the bodies of the soft palate split, and the muscles sutured. To carry such a delicate child through a repair of the extreme cleft without a bit of concern from the postoperative condition and with complete primary union all along the line is what I consider a great victory, and this extended description is purposely made to support the sequence of operation. This girl is now 7 years old, very diffident, and retarded in general growth, and it is difficult to test her speech. What came through, however, has a proper sound and her mother says she is readily understandable, which is not solid evidence to us, but she has at least a chance to improve, because the soft palate is movable. There was no chance to do a push back because a hole in the hard palate would be left and thus transfer a deficit behind to one in front. Should a gross speech defect become evident, the tissues are in position to follow the advice of Barrett Brown wherein the mucoperiosteum is split from before backward, leaving a covering of the cleft in the bone and the oral half pushed backward to increase the length of the soft palate. I have not done this but the enormous productivity of the mucoperiosteum is such that should occasion arise I would have no hesitation to follow Brown's technique.

Fig. 9a.

Fig. 9b.

Fig. 10a.

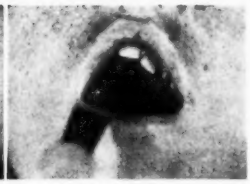


Fig. 10b.

Fig. 10. Group II, 3/3. This is the same case as in Figure 9 but in the adult, with the same aspect of a median cleft. The older patients, even with an extreme degree of the cleft palate, depending somewhat upon the intelligence quotient of the case, speak intelligibly, having, by means of the superior constrictor of the throat, tried to improve the speech. Such a case can be done under local anesthesia, but this case was done under general. The same operation

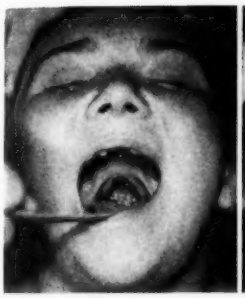


Fig. 11a.

Fig. 11b.

Fig. 12a.

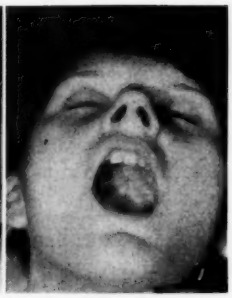


Fig. 12b.

Fig. 13.

as discussed in Figure 9 was done, but here the hamular processes were fractured, a step used only occasionally and carefully done, because the styloid process in the point of contact of the tensor palati and the superior constrictor and a gross disturbance of the muscle position causes another break in the great muscle scheme of the throat. This cleft at the junction of the hard and soft palate measured 2 centimeters, which is the widest degree I have ever found and one feels justified in using every measure to reduce stitch tension. The follow-up picture is not so good, but both hard and soft palates united primarily. The same problems on future care arise as are present in Figure 9. In this a very intelligible speech, even with the wide cleft, showed a notable improvement, but an outstanding result lies in the improvement in morale of the patient which stimulates her to improve her speech.

If surgery is ever justified on psychological grounds, it is in these cases of young women and men who come of their own volition or through some agency. Characteristic is an inferiority complex, and an attitude of profound unhappiness in being different from their fellows often makes an appealing picture. Even though the operative result may not be complete, the mere fact that something has been done and that someone has been interested in them has in so many cases changed the whole outlook on life.

Fig. 11. Separation of the line of suture in the palate may occur at any time, in any case and in any operation. Failure with loss of tissue is serious, through not so much in the hard palate. Years ago in a group II, 2/3, case the right mucoperiosteal flap sloughed out, but such is the wonderful recuperative power of this tissue that the loss was filled in, so that now, at 10 years of age, the outlines of the loss are obliterated. Loss of tissue in the soft palate is a tragedy, because this means loss of muscle elements which do not reform. This case is one of my cases in which the soft palate failed, with gross loss of tissue. I shall be eternally grateful to Dr. George Dorrance in having the initiative and courage to work out his push back and demonstrate that these tissues may be freely mobilized to accomplish closure: a, is the picture after the elevation and replacement of the mucoperiosteal flaps. b, is the result of the re-elevation of the flap, and its suture to the palate bone. The soft palate tissues were so loose that it was possible to dissect and remove scar tissue, to find and suture active tissue together, with a result which, with any other method, involves the risk of a second failure.

Fig. 12. A 16 year old girl who gave no history of previous operation, but the condition appears so alike that in Figure 11 that I feel that someone else obtained a failure of primary operation. I thought I would use the technique which was so complete and satisfactory in a cleft of similar degree to that used in case shown in Figure 8 b. In this case it was necessary to make an incision at the heel of the process for the insertion of New's elevator, the soft palate was then severed from the bone, the hamular process fractured, the lateral incisions extended to whatever degree is thought necessary. The incision was packed with dental cotton roll soaked in tincture of benzoin, cut to fill the incision snugly. The hard palate mucoperiosteum was sutured and the operation concluded, to be continued at another sitting, at which time it was found that the soft palate could be easily handled, the muscles found on each side and sutured together. The result was a primary union as shown in b. These older cases are most satisfactory because the patient knows what is being done for him and is most co-operative. Certainly the result in this case looks better than that in Figure 11, and was obtained by much simpler procedures which are applicable to secondary repairs as well as primary. In fact, I think I have unwittingly been doing a push back to some degree for many years.

Fig. 13. In about 4 in a hundred cases, a combination appears in which the lip is cleft, the process is normal and the palate is cleft, usually in the 1/3 or 2/3 degree. The lip is recorded as group I and the palate as group II. The clefts are repaired by the steps outlined previously in these two groups.

the right and left mucoperiosteal flaps, which must be sewn so that the periosteum is definitely in contact. I do this by using a lateral mattress stitch supplemented by single stitches in the folded ridge of mucous membrane. Mere contact invites defeat. Dr. Dorrance

has suggested that the mucoperiosteal flaps be skin grafted, a procedure which I have not carried out, because the field seemed too unfavorable for a "take." But the Veau operation works, and, although it is most applicable to the group III palate, I have had the courage to do it in two year old group II, 3/3, cases, without a bit of reaction and with perfect union of the palate. In fact, the operation on the hard palate produces no reaction. It is only when the two operations are done at one time that any concern is felt over the condition of the child or the outcome. The greatest satisfaction I have had is the recognition that two operations are involved, the hard palate and the soft palate, but my greatest difficulty is in deciding to close them at different sittings, and to do the hard palate first despite criticism of men of wide experience. Some of my colleagues shudder when I reveal what I am doing.

I think the Warren Langenbeck operation is a fundamental one and it is up to us to supplement it by modification of technique, age for, or sequence of, operation. The lateral sliding flaps on the hard palate, supplemented by the vomer flaps of Professor Veau, open up a vista of progress, which may end in a goal of success and answer the objections and erase the many personal opinions as to how it should be done and thus put a quietus on the effort to present some slight technical modifications, many of which are simply confusing to me. I have included in the pictures some secondary repairs because I have found that no matter what the meticulous effort, there are so many uncontrollable factors in the repair of cleft palate inimical to primary union that failure may occur at any point or all along the suture line.

Fig. 14a. Fig. 14b.

Fig. 14. Group III, left complete. In this case all the clefts are present on the left side, and thus the normally developed tissues are apart from the vermilion border of the lip to the uvula. a, Shows the most frequent case. The process cleft measures 8 millimeters. The average runs from 6 millimeters to 12 millimeters, below 12 millimeters down to a notch, above 12 millimeters up to 18 millimeters, which is the widest cleft on my records. This is the case on which I used to put the wires in the maxilla, with what seemed to me satisfactory immediate results. On account of observation of the babies' growth, I discontinued their use, because I saw so many cases grow up with narrow jaws, and malocclusion of the alveolar process with the mandible. This did not always happen, but enough cases of gross surgical deformity occurred to lead me to discontinue such methods in favor of manipulation and the construction of a movable active lip, which, by its action, exercises an enormous influence, not only on the process, but on the whole bony structure of the upper jaw. If by thumb pressure on the premaxilla, which is seen peeping out from behind the prolabium, the premaxilla can be brought down to the maxilla out of contact to 4 millimeters or less and the lip down over it, it is a constant observation to show the process closed by the time the stitches are removed from the lip. This happened in this case, because the premaxilla had healed on to the right maxilla quite symmetrically in the curve of the whole process. b, The postoperative picture as the baby left the hospital, with the vermilion border well alined, eversion of the mucous membrane and the floor of the nostril made with some irregularity of the left lower cartilage of the nose. This baby is a complete case, with primary union in the hard and soft palate, done in exactly the same way, as outlined in the group II cases. The process is closed and the lip has hardly a perceptible scar.

GROUP III. THE ALVEOLAR PROCESS CLEFT

THE GROUP III CASES

I once tried to find some percentages of incidence of the various combinations of the clefts, and while there were so many factors of error that no exact figures could be made, the indications were that most of the cases come with cleft alveolar processes. There are three subdivisions in this group, the unilateral, the bilateral, and case with a normal hard and soft palate. Broadly stated around 60 to 70 per cent of all cases appear in this group. The process cleft cases show the greatest variation in development and position of the frontonasal process. The maxillary processes, right and left, appear to be normally developed. In the bilateral clefts the degree of projectional displacement of the premaxilla and prolabium give a great variance to the picture of the case. In the unilateral case, the pivotal and rotational displacement of the premaxilla, healed normally to one or the other maxillary process gives the degree of the cleft, which in turn gives the great variation in the picture of the

Fig. 15a.

Fig. 15b.

Fig. 15. Group III, unilateral, left. This shows a case similar to that in Figure 14, but here the premaxilla has healed on to the right maxilla, with a definite degree of projection and rotation. I saw this baby at birth and put on adhesive straps extending outward on the cheeks and incorporated in the straps a rubber band, intending to get continuous traction in the curve of the normal process. The plan had some effect in narrowing the cleft to a point illustrated, a, but it was not complete. It was the same result that I obtained when I was using wire. Nothing really happened until the lip was done. At 6 months this case was manipulated and the lip done over a 4 millimeter cleft, with closure of the bone cleft. b, The lip looks about as usual, but the nostril is too wide open and the alar end of the cartilage too low. This boy is growing up with a flaring nostril, not of severe degree, but not perfect. This is also a completed case, with primary union in both hard and soft palate. The only question involved is the development of the nose.

Fig. 16. Group III, unilateral, right complete. This case is the reverse of that shown in Figure 15, with the same disposition of the tissues, except that the premaxilla has healed to the left maxillary process, in a position of at least 45 degrees' rotation. The outlines of the prolabium are not so definite. By reason of the rotation the columella is also decentralized. The nasal cartilage is extremely flattened. There is here also a choice of the preliminary use of wires and plates to close the process cleft forcibly, or the manipulation of the premaxilla and the reconstruction of the lip and nose, or the use of the vomer flap on the hard palate to be followed by the lip repair. The latter plan seems now to be popular and I have done it with varying ease and satisfaction, usually depending upon the degree of the process cleft. Such a procedure means two operations at one time. Since I believe that the use of the vomer flap is an accessory step in the closure of a hard palate cleft and can in no way substitute the median suture of the mucoperiosteal flap, and since I believe that a movable, functioning lip is essential to future growth, my tendency is to take the spring out of the bones, reduce the process cleft as far as possible and build the lip over it to complete the closure. b, This was done in this case. The operation of mobilization of the tissue, the muscle suture of the body of the lip, the construction of the nostril, and the centralization of the columella all require time and any extension of the operation seems to me to invite trouble. For these reasons I have often put off the vomer flap until the hard palate operation. Both the vomer flap and the suture of the mucoperiosteal flaps can be carried out at the same sitting without causing any shock.

Fig. 16a.

Fig. 16b.

Fig. 17a.

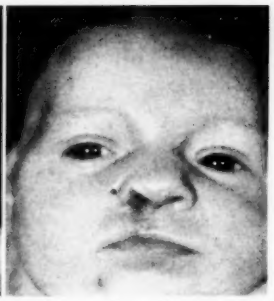


Fig. 17b.

Fig. 17. Group III, unilateral, right complete. Another case similar to that in Figure 15. The degree of the process cleft is entirely due to the pivotal displacement of the frontonasal process and of course, the left maxilla in this baby is displaced outward secondary to the position of the vomer and premaxilla. To move the premaxilla and the whole maxilla requires positive force, and in a 14 millimeter cleft it is never complete and has a tendency to spring back. I have faithfully used outside force, by adhesive straps and rubber bands, and a suggestion made by Dr. H. R. Allen of Indianapolis in which a clock spring instead of the rubber bands is incorporated in the adhesive strap. I have been able to gain as much as 6 millimeters, but there never was complete closure by such methods. So tragic were the late results in those cases where I used direct force through wire, that I have promised myself never again to insert them in the upper jaw, but I have wondered what penalty would be paid in putting in some material to hold the premaxilla down until the lip was done. Of course, such a wire or silk worm would encircle the premaxilla and thus possibly inhibit circulation to the front incisors and interfere with their normal development. When I first suggested the circular wires applied in the curve of the process, Dr. W. H. Logan of Chicago made this criticism and I am able clinically to support his contention. I believe it better to take a chance of manipulation of the premaxilla and lip repair. If the process cleft is not closed, it is possible later in life to insert a lateral incisor, which so often comes in deformed anyway. b, Compare this nostril with that shown in Figure 17 a. The cartilage is nicked, the floor of the nostril was better than the picture because it was not cleaned off. Can anyone explain why in one case the outcome is acceptable and in the other deformed?

Fig. 18a. Fig. 18b.

Fig. 18. Group III, left complete. Secondary repair. The muscle theory repair of the lip fits perfectly into the secondary repair of the lip. a, Shows an incomplete repair with a flaring nostril, no floor to the nostril, a notch at the vermilion border, and what looks like the result of the old harelip operation. To prevent such results many operations have been devised. The lip must be broken down and the scar tissue removed to find the ends of the active tissue and the technical steps followed as outlined in Figure 1.

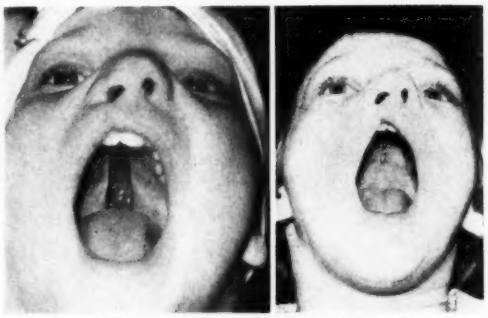


Fig. 19a. Fig. 19b.

Fig. 19. Group III, right complete. This case is included because the girl shows unacceptable results in both the lip and hard palate. Her chart shows originally a 10 millimeter cleft process and a 14 millimeter measurement at the junction of the hard and soft palate. The process was manipulated and the lip done. She was quite sick, the upper stitches of the lip became inflamed and the wound separated. The lower stitches of the lip pulled, with the resulting deformity of the nose and floor of the nostril and the red border included in the lip wound, a condition similar to that in Figure 18a. So concerned were the family that she did not return until 5 years of age. The process cleft was closed and the front incisors appear normally placed. The measurement at the hard and soft palate was now 10 millimeters, i.e., in the interval, by waiting, the tissues of the hard and soft palate were brought 4 millimeters nearer to each other, either by growth or indirect pressure of the coordinated expression muscle groups, or simply by weight of the soft tissues of the upper jaw, or all these factors together. I have seen this occur quite constantly, and if others support the observation it may be an argument in support of Dr. Dorrance's opinion that the cleft palate should not be repaired until the age of 4, 5, or 6 years, at which age it would be expected that the maxillae are fixed and set to resist any possible effect of scar formation or contraction on their normal growth and thus meet the objection of the dental surgeons. At this age also it may be reasonable to do both hard and soft palate operations at one sitting, as was done in this case. The Veau flap would be difficult to cut, if not impossible in this case. In 19b, the hard and soft palate closed primarily. The hard palate shows the projecting ridge built up by the lateral mattress stitch used to bring the periosteum in contact. This usually disappears as in Figures 6, 7, and 8, but once in a while it stays with no disability except that of a cosmetic deformity. The soft palate is long, flexible, and has perfect function for speech. This was a public case and such was the attitude of the family that it is difficult to get them to consent to further surgery, but I predict she will come of her own volition later to have lip and nostril corrected.

palate, while in the lip the width of the cleft is entirely secondary to that of the process cleft. The picture of a median cleft palate is lost, although in the bilateral case it is often evident.

While the lip and palate problems are present, they are in more extreme degree than in group I and group II, but added to them is a bone cleft around the proper care of which has raged the greatest diversity of opinion. In fact, the group III, unilateral, being the most frequent combination of the clefts, has been the subject of most of the literature. This case has been called the single complete harelip and cleft palate, which fairly describes most of the cases. This description puts the alveolar process into the palate, and the treatment of this cleft has been included in the procedures called cleft palate operations. The embryology indicates, however, that the alveolar process is formed in relation to the lip, and therefore the care based on the idea of a whole or complete cleft palate is an incorrect premise.

Because of the fact that the process cleft was evidently in the bone, the idea was carried to the whole palate, and since bone is the most resistant of all tissue, some kind of force is necessary to move it. Hence there appear in the literature many plans, all collected by Dorrance in a chapter called "Uranoplasty by Compression Methods." The late Dr. Brophy was the outstanding sponsor of the use of compression methods and his ingenious plans are given in a special chapter in the "Operative Story of Cleft Palate." So influenced was I by his theories, arguments, and practical experience that I undertook to follow his suggestions and I have not yet recovered from my surprise that the cleft palate was not closed, and

Fig. 20a.

Fig. 20b.

Fig. 20c.

Fig. 20d.

Fig. 20e.

Fig. 20. Group III, with a normal palate. In about 10 to 20 per cent of the cases there is a case of cleft lip, a cleft process, and a normal hard and soft palate. These cases are the clinical support of the embryological fact that the alveolar process is not a part of the palate, but has a definite origin of its own, and is formed in relation to the lip. In most of these cases, the alveolar process cleft is not wide and the case often presents the problems of group I, prealveolar cleft, but on about 4 occasions I have had a case in which an apparent overgrowth of the premaxilla presented an added problem in repair. I present this case because it brings up a problem once discussed in the literature—the removal of the premaxilla. In a, it is to be observed that the processes of the right and left maxillae are near together with only a small triangular space between them, in perfect shape and position to receive the premaxilla, had it not been so large and so projectionally displaced. This triangular space is only evident in this combination of the clefts. In the embryology apparently the fore part of the palate is filled in, not by mucoperiosteum, but by tissues developed in the frontonasal process, which is another argument for the Veau vomer flap. Clinically I have found that the vomer flap is most satisfactory for the forward third of the palate, but if the flap is used as a lining for the mucoperiosteal flaps, it should be carried back as far as possible, which I think is all right, provided the mucoperiosteum is sutured at the same time. Unless this is done in the hard palate and the operation continued to include the soft palate at the same time, it is impossible at a later date to sever the soft palate from the horizontal plate of the palate bone without disturbing the vomer flap, and in some cases I have had to undo the first operation. In b, the extreme projection requires a repositioning of the premaxilla, but in this case the size of it was too large to fit into the triangular place, even if it could be pushed back, so I decided to do the lip and see if the rest of the face would grow up to the premaxilla. In c, the result of the lip repair. Both sides were done at one sitting. d and e, I let her go until school age, but her deformity was so terrible that I decided to remove the premaxilla and have a premaxilla built on a denture later. This is the only time I have removed a premaxilla, although at one time this procedure was advocated by distinguished surgeons. Of course, it should not be removed, except for some such reason as has been stated. e, Shows the process cleft still present. I have similar conditions in the unilateral case in which the indirect force of the lip has not closed the bone cleft, either due to the width of the cleft or the rigidity of the bones in the case, and a similar deformity is left. It is such observations that have led me to advise that all cases of alveolar process cleft be attacked at an arbitrary period of 6 weeks—at least before 3 months of age, while the bones of the jaw are still soft and pliable, not on account of the lip or palate cleft, but on account of the process cleft.

that the main achievement was the closure of the alveolar process cleft. The hard palate and soft palate subsequently had to be repaired and, although the cleft appeared narrowed, it was necessary to mobilize the hard palate and denude the soft palate. I have found the report of no case in which the palate has been closed by compression methods. The methods incurred in my hands a penalty of overcorrection that seemed to be a worse deformity than the original condition, but I still felt that some form of direct force was necessary to close the cleft in the process and proceeded to suggest a plan which purported to influence this cleft. The results were so poor that I revised the whole chapter in order to pull out this part on compression methods. Dr. Dorrance complimented me by including the plans in his book, and, although I think the arguments for it are logical and theoretically correct, practically the results were terrible and I shudder to think of the babies whom I have subjected to such methods. However, the hard palate and soft palate techniques have held up with such constant satisfaction that I resubmit them. But should anyone be interested enough to review that part about the wires applied to the upper jaw, please consider it blacked out.

Fig. 21a. Fig. 21b. Fig. 21c. Fig. 21d.

Fig. 22a. Fig. 22b. Fig. 22c. Fig. 22d.

Fig. 21. Group III, bilateral. a, In most of the cases the premaxilla is centrally placed and here is the picture of the most frequent case. I early found out that there is no muscle tissue in the prolabium, and yet in the normal lip there is muscle. At first I did both sides at one operation, and I found that I could obtain a satisfactory skin closure without crossing stitches, but the results all looked to me like curtain lips. So I decided to do one side at a time and try to bring the muscle bundles to the midline of the prolabium and, at a later date, do the same thing on the other side, that is, do two unilateral lip operations at different sittings. The attempt is made to incorporate the prolabium in the lip. This is in direct opposition to the opinion of many surgeons of wide experience who believe that the prolabium is a part of the columella. b, The result of the first operation on the left side, in which the slight rotation of the premaxilla is overcome by the force of muscle pull. c, The picture of the lip as the baby returns for the other side, after a 6 weeks' or 2 months' interval. d, The lip completed, with the right and left expression groups, if not in contact, at least anchored in the direction of the normal action. This case was completed by doing the hard palate in the next step and then the soft palate, as outlined in the group II cases.

Fig. 22. This is another average case, with a bit more projectional displacement of the premaxilla. The prolabium is well developed, but does not move on electrical stimulation. It is about the limit where it may be expected that the lip will completely bring the premaxilla down to the maxilla on either side. One may try to learn by thumb pressure how near the process clefts may be closed. The trouble is that the premaxilla may spring back, or if the distance is too great, a bend in the vomer and septum occurs which may be of such degree as to obstruct the nasal channel. If this occurs, the vomer must be sectioned. There are several ways, and I have tried them all, and have discarded any procedure that entails removal of any part of the vomer. The square piece or triangular piece removed just back of the premaxilla has been discontinued because not infrequently this step resulted in a movable premaxilla, but the main reason was that it caused an inhibition of growth and atrophy of this essential structure of a normal process. I have cases growing up in which the premaxilla has failed to develop to a point that looks as though I had removed the premaxilla. I have tried removal of a square piece from the middle of the vomer, and although the premaxilla develops normally there still may be free motion of it. So I have selected to fracture the vomer about the middle, by reflecting the mucous membrane back, exposing the vomer. The fracture is made with a chisel and in as oblique a manner as possible. This permits sliding the forward half backward on the posterior half. The direction of the cut shall be pointed forward to the cleft opposite to the lip cleft which is to be repaired. In this case it was directed to the left cleft, and the right cleft lip repaired. b, The pull of the right facial group on the prolabium and the columella is well shown. This pull is also on the whole forward half of the vomer, to hold the raw surfaces together, and it is the greatest satisfaction to find that in Figure 22c bony union of the fracture has taken place. The premaxilla is replaced in contact with the maxilla, surely on the right side and almost on the left. The picture shows the muscle bundles of the right side tucked in under the prolabium. It is not possible to do this so well in all cases, but that is the purpose. c, Shows the result of the second operation on the left side, which also completed the closure of the process cleft. d, Shows the boy as he returns for the hard palate, to be followed by the soft palate at a later date. The pro-

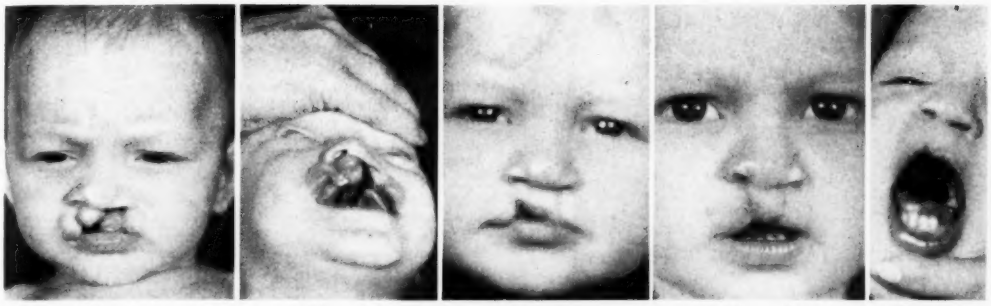


Fig. 23a. Fig. 23b. Fig. 23c. Fig. 23d. Fig. 23e.

labium has had a chance to grow. One may criticize the width of the nostrils and the depression of the tip of the nose, but there is a look of comfort which I believe is due to the fact that his expression group of muscles have been co-ordinated.

Fig. 23. a, This case shows the extreme pivotal displacement of the frontonasal process to the right. The baby just missed being a left unilateral case. The not infrequent picture of the tongue lying in a process cleft has been used in support of the proposition that in the etiology of these clefts, interposition of the tissues is a factor. In the lip the tissues of the right maxilla are partially in contact with the prolabium, with probably some muscle fibers migrated over, so it is quite constant to obtain some motion in the prolabium by electrical stimulation. b, The premaxilla is in contact with the process of the right maxilla, doing so by rotating to the right. The projection is not great and a removal of a piece of the vomer may pay a penalty of replacing the premaxilla too far back. It has now become the form to do the Veau vomer flap on one side and the cleft lip on the same side at the same sitting, thus presenting another reason for doing a bilateral lip, one side at a time. This reason is different from the one upon which I have been working, which is that I have found it the easiest and most direct way to line up the muscle bundles underneath the prolabium and thus co-ordinate the right and left facial groups of muscle. In other words that the bilateral lip is simply two unilateral clefts in one case. In this case, I elected to reflect the mucous membrane of the vomer and obliquely fracture it about the middle with a chisel. The forepart of the fracture pointed to the incomplete cleft of the process and lip and I proceeded to do the left lip cleft. c, The picture of the baby when it returned for the right incomplete cleft, with the premaxilla centered and the vomer rigid. The right nostril is too wide, and although the lower nasal cartilage is improved, it is not perfect. It is most difficult to line the vermilion border exactly. Apparently the line is perfect on the left side and incomplete on the right, but the lip appears normally prominent. d, The picture of the lip and nose as the baby goes home after the first palate operation. The immature prolabium in Figure 23a has grown downward. The vermilion border of the prolabium is a part of the red border of the lip. Any divergence from the normal is purely a technical result. c, The palate shows the result of suture of the mucoperiosteal flap and the complicated palate has been changed over to the group II, 1/3. Everything is done except the suture of the soft palate muscles. This was done later, with primary union.

In this case the use of the Veau flaps before the premaxilla was centered or done in conjunction with the lip would have carried a risk of failure. But of course it is easy to line the suture of the lateral sliding flaps. I have found that the vomer mucous membrane heals kindly after the vomer fracture, but of course both operations, the fracture and the Veau flap cannot be done at one time, so in these extreme cases the problem of sequence of operation is most important.

GROUP III. BILATERAL

In these cases the right and left maxillary and the frontonasal embryonal processes are out of contact all along the line. The consideration of the subject should really begin with the study of them because all combinations and degrees of clefts in the group I, group II or the unilateral subdivisions of group III are simply exhibitions of failure of contact of these three embryonal processes at this or that point, or complete union of the normal, or complete disunion as here shown. With this picture in mind, it is possible to determine in any case what has or has not happened in that case, and with the picture of the normal baby in mind, one is in a position to decide what should be done surgically to correct the defect. Of all of the parts involved, the greatest variations in development and position are not in the lip or the palate, but in the vomer and premaxilla. The vomer at times is sturdy, again thin and wafer-like. In the unilateral case the vomer mucous membrane may be widespread, a definite structure easy to handle, or thin and delicate, difficult to handle without perforation. The premaxilla shows wide margins of projection, as in Figure 17b, or extreme rotation on its stalk. The prolabium of the lip may be small and undeveloped to a point where it seems hardly worth while to use it, or it may be a definite structure with sufficient body to hold stitches.

Fig. 24. Two cases of bilateral lip repair are compared. In a, left, operation was directed to repair of the lip and the reconstruction of the nose was secondary. In b the purpose was reversed. These 2 cases are presented in support of an observation that the repair of a complete cleft of the lip, both unilateral and bilateral, entails the consideration of two operations divorced in principle, viz., in a, an anatomical replacement of active tissues out of contact in the lip, with function a prime purpose, and in b, a plastic repair of inactive tissues of the nose, with cosmetic result a prime purpose. These are surgical principles recognized elsewhere in the body, but ignored in this field. In b, the surgical principle of the nose repair is carried to the lip, the mucous membrane of the prolabium is sacrificed, and the maxillary tissue sutured below the prolabium. b, is only one of the results of trying to place the prolabium of the lip into the nose.

I can show cases in which the prolabium, left in the lip, having no place to grow, has humped up like a mattress. I can show cases in which the maxillary tissues below the prolabium have grown so that the lip became inordinately long, but most of the b cases are curtain lips. Figure 24b shows the boy, showing the limit of his motion. He has a flap upper lip due to the fact that the muscle bundles have not developed, because it is repeatedly demonstrated that muscle tissue atrophies on disuse. In Figure 24a, I felt that I had a definite purpose in replacing the tissues according to the embryology, the position of the parts supported by clinical results in the group I cases and the group III unilateral cases, while in b I was simply doing something on my own hook. In a, an unsatisfactory result would be a technical fault. In b, an unsatisfactory result would be due to a failure to recognize surgical principles. Every evidence points to inclusion of the prolabium into the lip.

SUMMARY AND CONCLUSIONS

The series of cases here presented gives one only a glimpse of the many combinations and degrees of the cleft which present themselves for correction. These cases were not selected to show good or bad operative results, but each case shows average degrees and combinations and in the main are presented to indicate the applicability of the classification to describe the case. Comparison of the group I and group II cases with the group III cases clearly supports a proposition made in 1920, viz., the alveolar process is a basis for the surgical grouping of these cases. I believe that the most important requirement of progress in this field is some kind of nomenclature and descriptive terms to substitute the loose and indeterminate terminology of harelip and cleft palate which permits the same case to be described in several ways according to the opinion of the observer. The special term "harelip" is misleading and has fostered the presentation of operations, which, on analysis, are simply plastic procedures which represent the personal opinions of the sponsor, as to how the operation should be done. "Cleft palate," is also misleading, as its use is made to describe a whole palate and thus fails to indicate the presence of several kinds of tissue. No direct mention is made of the alveolar process, the condition of which is so important to the case. With failure to recognize the character of the structures involved, we have the Langenbeck, the Lane, the Brophy, the Veau, the plan sponsored by Dr. W. B. Davis, and the Dorrance push back operations and their modifications for cleft palate. The presence of a cleft alveolar process produces a startling picture, but I see no reason to believe that the conclusions of the group I lip and their forms and degrees are directly due to the disposition of the muscle elements or the conclusion of the group II case, that the clefts of the hard and soft palate are median clefts or that the character and texture of the tissues are changed because of the presence of a factor entirely outside their structure. Because of the dual point of view of harelip and cleft palate, I find contributors interested in one or the other. I believe we should be interested in the case as a whole, to study it as an individual and to select a procedure which will not exceed the possibilities of the tissues in mobilizing and suture. I early decided that the way to close the clefts was already in the literature, and, although other operative steps have been suggested in the past few years, these newer ones, the Dorrance push back and the Veau vomer flap, while gratefully accepted, appear to me not fundamental changes, but accessory steps which it is possible to do, not as a rule, but in selected cases, the push back applicable to the

group II, 1/3, case, the vomer flap to the group III unilateral, where it may be used for three reasons: to close off the nasal canal, to fill in the triangular space back of the premaxilla, and to line the mucoperiosteal flap. It is acceptable on all counts, but the fundamental requirement in the repair of a cleft hard palate is the suture of the mucoperiosteum. In many technical operations a fundamental principle in wound repair, layer or series sutures, is ignored. The fact that transfixation sutures narrow the contact of denuded surfaces is not considered. This is seen in the soft palate, as in the Brophy operation or in the old harelip pin operation for the lip, wherein the contact of the body of the lip was narrowed and only mucous membrane and skin were united. Also in the hard palate, the flaps of which are composed of two of the most vital tissues in the body, mucous membrane and periosteum. Warren probably sewed the periosteum but did not mention it, and it remained for Langenbeck to indicate its importance. In spite of this, I have seen the flaps sutured in the midline with a continuous running stitch, or with delicate needle and suture material, which may or may not include both tissues. It is wise to be sure, because the end-on or vertical mattress, or better, the lateral mattress for one series sutures plus single stitches for the raised up mucous membrane are exact. Sometimes it is overdone, but usually it smooths out, as in the group II palate.

I can remember only one case in which the lateral incisions did not promptly heal in. Of course, the dental surgeons and their reports on the growth of the upper jaw are most disturbing about median closure of the hard palate, and two proposals must be considered: first, the use of the vomer flap to line the mucoperiosteal flaps, or a postponement of the hard palate operation until patient is 4 or 5 years old, as so definitely advised by Dorrance. At that age the maxillae would probably be so set that any contracture would not influence the future growth.

And so I conclude the presentation, feeling that many phases of the subject have not been covered and that much repetition has been made. It was difficult to curb the desire greatly to augment the number of cases shown because, in reviewing the records, each case has some special story of experience and results. After 25 years of interest in this subject and the care of over a thousand of these cases, I believe that the future progress depends upon the discussion of and agreement on surgical principles. Based on the findings in embryology, anatomy, and physiology as outlined in previous discussion (5), and the clinical presentation here made, I repeat some principles upon which to work in the future:

1. The approach to the subject shall be changed over from the dual point of view of harelip and cleft palate to the idea of a series of congenital clefts which involve the face and jaws.

2. The lip cleft shall be approached as a break in the great muscle scheme of the face, which involves the consideration of two separate operations: an anatomical replacement of the active tissues of the body of the lip plus a plastic repair on the inactive tissue of the nose.

3. The alveolar process is a definite entity of as much importance if not more so than the lip or the palate. It is not a part of the palate, so that the compression methods, such as the Brophy cleft palate operation, have been established on an incorrect premise and should be discontinued. The complete cleft palate of the literature is a combination of two clefts involving the handling of bone tissue in the process plus a plastic repair on the inactive tissues of the hard palate.

4. The soft palate cleft is a problem similar, if not identical, with the lip cleft—an anatomical replacement of active tissues out of contact, and the cleft of the soft palate is again simply a break in the great muscle scheme of the throat. Contrary to the lip cleft, it is possible to identify a muscle such as the tensor palati, the precise suture and union of which is a great essential to successful function of the soft palate.

I early concluded that the muscles of the soft palate did not work against the bone, but against the tensor palati, and it made no difference where the tissues of the soft palate were, so long as this muscle was united. In order fully to identify it I found it necessary to sever the mucous membrane attachment of the soft palate to the horizontal plate of the

palate bone. Thus, after accepting and performing the push back of Dorrance and comparing results, I think I have unwittingly been doing the push back for many years. However, the point of importance is that the operation I have been doing is applicable to the group III palate as well as the group II palate. My greatest unsolved problem is to construct a deformed nostril to look and grow like the normal one.

REFERENCES

1. [1]DAVIS, WARREN B. Pennsylvania M. J., 1939, 43: 153–158.
2. [2]DORRANCE, G. M. The Operative Story of Cleft Palate. Philadelphia: W. B. Saunders Co., 1933.
3. [3]IVY, R. H. Ann. Surg., 1940, 112: 775.
4. [4]KILNER, T. POMFRET. St. Thomas's Hosp. Rep., London, 1937, vol. 11.
5. [5]RITCHIE, H. P. Congenital clefts of the face and jaw. An attempt to correlate the embryology, anatomy, and physiology of the structures of this part of the body to the surgical requirements of the repair of this deformity. Vol. 5. Chap. 9. Practice of Surgery. Edited by Dean Lewis, M.D., Sc.D. Hagerstown, Md.: W. F. Prior Co., Inc., 1930.
6. [6]SCHREINER, E. OLIN. Clinics of the Virginia Mason Hospital. April, 1938.
7. [7]STRAITH, CLARENCE E., and DEKLEINE, E. HOYT. J. Am. M. Ass., 1938, 11: 2364–2370.
8. [8]VAUGH, H. S. Congenital Cleft Lip, Cleft Palate and Associated Nasal Defects. Philadelphia: Lea & Febiger, 1940.
9. [9]VEAU, V. La division palatine. Paris: Masson & Cie, 1931.

[1]Davis advocates the inclusion of the palatine process in the lateral sliding flaps, which are mesially sutured with interrupted wire sutures, thus erasing the possibility of scar formation which may interfere with development of the upper jaw, a late development when the mucoperiosteal flaps are raised from the bone as in the Langenbeck.

[2]The outstanding contribution to this subject in recent years, in which Dorrance has collected and filed the operations presented from the beginning of accessible literature with historical comments and a complete bibliography. He presents an original operation for the group II palate.

[3]Ivy quotes Axhausen and presents his diagrams. He also presents diagrams from Veau. He reports the use of a combination Axhausen and Veau in the group III unilateral and bilateral cases and the Axhausen in the group II cases, with specific statements of the age for operation. This is a very valuable paper, not only in the form of the presentation but in the reasonableness in conclusions and performance.

[4]Beautifully written and illustrated paper of operations he has selected and done, with logical reasons for their choice.

[5]An effort which purports to change the approach to our various problems from a viewpoint other than that of hare lip and cleft palate.

[6]Defines early closure as operation in the first month of life and late closure to be after 3 months. Shows several cases done at 12 hours and at 2 days, with excellent postoperative results.

[7]Advocates early lip repair, the first day or first week.

[8]A concise, yet complete and very orderly presentation of the subject, with diagrams and clear discussion of the many lip operations, as well as the process and palate procedures, which recognize that the alveolar process cleft is an entity separate from the hard and soft palate.

[9]This is but one of a series of monographs written by a master surgeon. Others deal with the lip repair, one on the embryology and on other phases, so that the series covers most of the field. With the war disrupting channels of communication, these pamphlets have increased value. I have them on file in the library of the Ramsey County Medical Society in St. Paul.

THE TREATMENT OF COMMINUTED FRACTURES OF THE OS CALCIS

W. RUSSELL MacAUSLAND, M.D., Boston, Massachusetts

THE problem of treating the *crush* fracture of the os calcis with displacement and comminution into the joint is well appreciated, as is evidenced by the numerous contributions to medical literature dealing with the reduction and end-results of this fracture. From the many methods of treatment advocated as well as from the variable results, it may be concluded that no method proves entirely satisfactory in all cases.

On the other hand, there is no doubt that definite progress has been made in the treatment of these fractures during the past decade, and studies of end-results show an appreciable decrease in both the temporary period of incapacity and the amount of permanent disability.

In connection with the treatment of these severely comminuted fractures, the question arises as to whether perfect function can be restored in all cases by any method. The subastragalar joint involved is a weight-bearing joint, and the integrity of its articular surface is vital to the mechanics of walking. It is difficult to secure accurate replacement of the individual fragments, and in the event of imperfect alinement, the joint no longer functions properly and arthritic changes subsequently develop. Even when an apparently exact restoration of the joint surface has been obtained, arthritic changes develop as the result of periarticular damage and from bearing weight on the roughened joint surfaces. Another factor to be considered is that these fractures occur almost exclusively in working men, many of whom before sustaining the fracture have a "wear-and-tear" arthritis. A perfect recovery cannot be expected in such cases any more than in severely comminuted fractures of the ankle or knee-joint that are complicated by arthritic changes (Figs. 1 and 2).

From the MacAusland Orthopedic Clinic.

At the present time the methods of treatment in use range from simple immobilization without reduction of the fracture, through dislodgment of the fragments by manipulation or by a crushing force and molding of the fragments into position, through traction measures, to operative reposition or early arthrodesis. Plaster fixation alone is no longer considered an efficient form of treatment, and the great majority of surgeons are of the opinion that an attempt should be made to reduce the fracture. A survey of a series of cases that were originally treated by plaster fixation, and years later were seen at our clinic, showed clearly the inadequacy of this treatment. There were 43 fractures in the series. All patients, with the exception of a few who had a solid ankylosis of the subastragalar joint, were permanently disabled. The deformity persisted, the os calcis being shortened and broadened and pulled upward. The patients complained of sore, painful, and tender feet and of restricted motion. Not one of the patients had been able to resume his former occupation, but several were doing a lighter form of work.

Reduction by manipulating the foot over a vertical bar and molding the fragments into position (Yoerg) may be difficult because of the great force required to free the fragments and pull the tuberosity downward. The dislodgment of the interlocked fragments by the blows of a hammer (Hermann and Pretty) would appear to subject the os calcis to a traumatic and uncontrollable force. However, both the manipulative and hammer methods have a certain following, and good end-results have been reported in fairly large series of cases.

Operative reduction has been advocated particularly by French surgeons (Lenormant and Wilmoth) as the most satisfactory treatment when the fragments that include the subastragalar articular surface are depressed

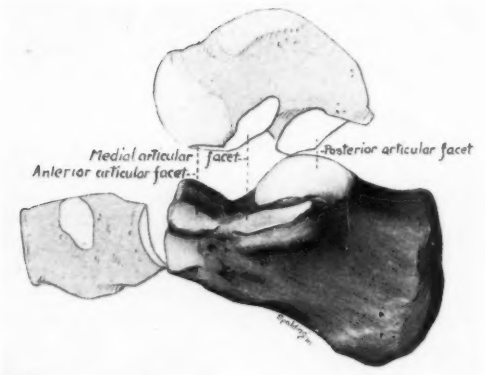


Fig. 1. The three articulating surfaces of the os calcis and astragalus. Viewed from the medial aspect.

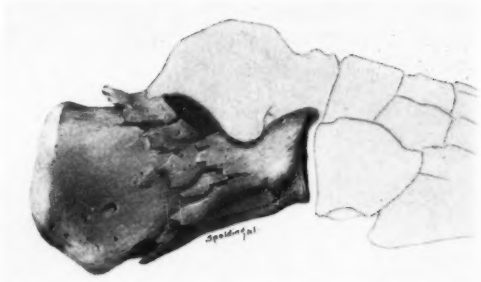


Fig. 2. The typical squash-type fracture of the os calcis with disruption of the joint surface. Viewed from the lateral aspect.

into the body of the os calcis. Recently Murray advised this procedure in such fractures. The operative method consists of elevating the upper cortex of the bone to restore the articular facets to normal position, and securing fixation of the replaced fragments by means of a metallic osteosynthetic material or by osteoperiosteal grafts. The method obviously has a limited field of application; it necessitates operative trauma and hence more atrophy; and it is difficult to pry fragments bearing articular facets into normal position and insure their fixation.

Arthrodesis has a place in the treatment of comminuted fractures of the os calcis, not as a primary measure, but as the treatment of fractures of long standing with persistent pain, sensitiveness, and restricted motion, in which conservative procedures proved ineffective. The fact that many good functional results are obtained by reduction is an argument against the immediate sacrifice of the joint. There are, furthermore, certain contra-indications to performing an arthrodesis in fresh fractures; not only is it difficult to carry out the operative technique in the presence of disorganized articular surfaces and damaged tissues, but also there is the danger of infection.

Of all forms of treatment, traction methods are the most generally accepted. The outstanding traction method is that advocated by Boehler, and more comfortable, weight-bearing, and functional joints have been obtained by this method than by any other procedure (Stewart, Carothers, Jaekle and Clark, Schofield, MacAusland). An alternative method of traction that is finding favor in Germany has been used by Ehalt and by Westheus. It consists of introducing a transfixion pin into the posterior fragment of the tuberosity and using it as a lever to force the tuberosity downward. Lateral deviation is overcome by means of a compression clamp.

The technique of the Boehler method is so well known that only a few features will be emphasized. In brief, the method consists of (1) freeing the interlocked fragments by manipulating the foot at the subastragalar and midtarsal joints, (2) restoring the normal so called tuberosity-joint angle by traction, (3) restoring the length of the os calcis by traction, (4) correcting the lateral broadening by means of a compression clamp, and (5) maintaining fixation and protection until union is firm. In the dislodgment of the fragments, as complete motion as possible should be obtained in the subastragalar and midtarsal joints. If necessary a Thomas wrench, or a wooden wedge over which the foot is buckled, may be used to secure free motion. Traction is established by means of two transfixion pins and the Boehler screw traction apparatus. Some objection has been raised against introducing a transfixion pin in the comminuted os calcis because of the danger of the development of infection or an osteitis, but these complications have not been encountered in the experience of the writer.

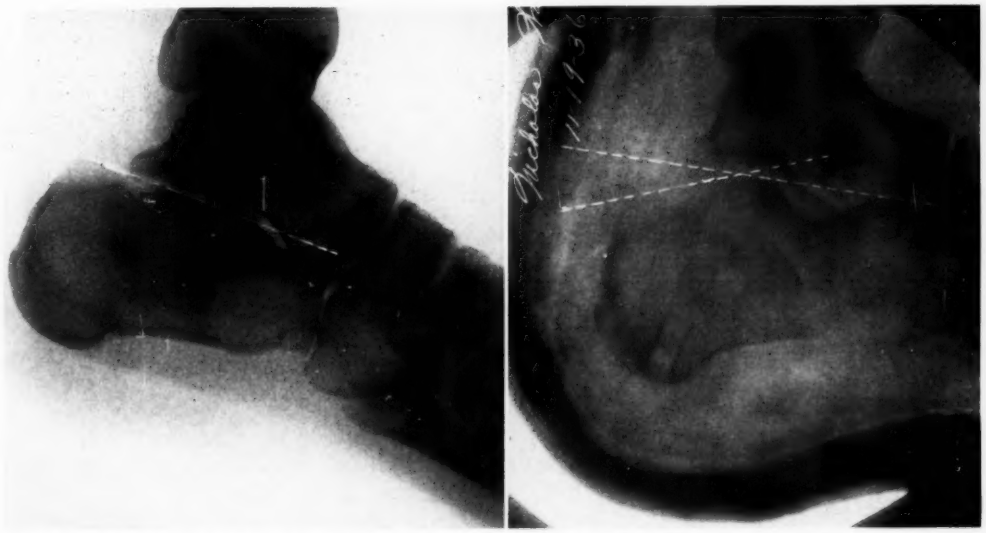


Fig. 3. a, left. Case 6 N. W. Comminuted fracture of the os calcis involving the posterior articular facet. Obliteration of the tuberosity-joint angle. b, The foot in a plaster cast following reduction by the traction method. Note the restoration of the normal tuberosity-joint angle in this case.

Following reduction, it has been the custom at our clinic to continue traction with the leg on a Braun splint for about 3 months. Upon the removal of the traction, a light walking plaster cast is applied with pressure pads under the malleoli, and worn for about 6 weeks. A shoe with an outer upright brace is then used for protection. This method has been used to maintain reduction, in preference to a plaster cast with the pins incorporated, which permits early walking, for two reasons. A great deal of damage to the tissues, extensive hemorrhage, and swelling are associated with these fractures. It is the writer's opinion that the foot more quickly and more surely returns to normal when it is kept elevated and at rest during the first few months of treatment. Then, too, when a plaster cast is applied soon after reduction it becomes loose as the swelling subsides, allowing deformity to recur.

One of the problems in treatment is the atrophy of the tarsal bones from prolonged disuse, which causes the foot to be sore and painful when weight-bearing is started. Such atrophy is easily overcome if the patient cooperates and uses the foot.

REVIEW OF 22 CASES TREATED BY THE BOEHLER METHOD

During the past decade, traction has been used exclusively in our clinic as the method of treating the troublesome squash-type of fracture. The series of 22 cases includes only those cases in which at least 1 year has elapsed from the time of treatment, and in which it has been possible to investigate the end-result. Eleven of these cases were analyzed in a report published previously (8), but these patients have again been examined, and the findings correlated with those of the new series.

All except one of the patients were males, and the majority of them were between 30 and 50 years of age. The fractures had been the result of a fall from a height while the men were at their work as carpenters, telephone repair men, construction men, or laborers. All the fractures sustained were comminuted into the subastragalar joint, with disruption of the articular surfaces, telescoping of the fragments, and lateral bulging below the external malleolus. Reduction was carried out within 4 days of the injury in all cases except one, which was complicated by shock.

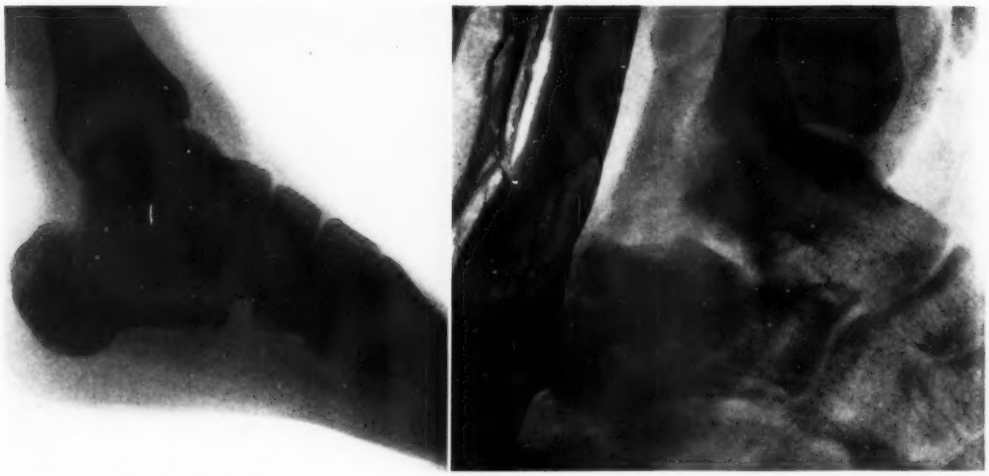


Fig. 4. a, left. Case 10 S. M. Comminuted fracture of the os calcis with the posterior articular facet crushed into the body of the bone, displacement of the forward fragment with the anterior facet, and loss of the tuberosity-joint angle. b, Reduction by the traction method, showing the tuberosity-joint angle slightly overcorrected.

The 22 patients were examined at periods varying from 1 to 9 years after treatment. The postoperative periods may be summarized as follows: 1 year, 2 cases; 2 years, 1 case; 3 years, 1 case; 4 years, 4 cases; 5 years, 4 cases; 6 years, 3 cases; 7 years, 1 case; 8 years, 2 cases; 9 years, 4 cases.

Evaluation of the end-results on the basis of the recovery of a comfortable, weight-bearing, and functional joint that allows the patient *to return to his former occupation* showed uniformly good results. Nineteen of the 22 patients returned to their accustomed employment, and in this group were carpenters, heavy construction workers, laborers, and telephone repair men. Four bilateral cases were in this group. Work was resumed in most cases within a period of from 5 to 9 months after the fracture. There is, of course, the psychological factor to be considered in estimating the period of incapacity in cases that involve compensation.

These patients walked without a limp, and they experienced little discomfort, even after

Fig. 5. a, left. Case 5 D. R. Comminuted fracture of the os calcis with marked upward displacement of the entire posterior fragment. b, Roentgenogram taken 4 years, 9 months after reduction by the traction method. Note correction of upward displacement of posterior fragment and restoration of normal tuberosity-joint angle.

hard work. Seven patients complained that the foot felt tired after prolonged standing; 1 patient experienced pain when walking on uneven ground; 1 complained of pain in stormy weather; and 1, of stiffness in the morning. The only residual disability was a loss of motion in eversion and inversion from one-third to one-half, but this restriction in itself was not disabling. Two patients had a slight lateral thickening below the external malleolus.

The roentgenograms at the time of the final examination showed that the plane of the joint surface had been restored to normal, and in only 2 cases was there any thickening below the external malleolus. In several roentgenograms there were changes at the subastragalar joint that were suggestive of a fibrous ankylosis, but such findings are to be expected in these severe fractures in which the articular surfaces are destroyed. Illustrative roentgenograms of 3 cases taken before and after reduction are seen in Figures 3, 4, and 5.

There were 3 poor results. One of the patients was a carpenter who sustained a bilateral fracture, and that on the right foot was treated by the traction method. One year after the fracture, an arthrodesis was necessary to relieve the painful arthritis. The second patient is now suffering from an arthritis involving both the ankle and subastragalar joints, and the third patient complains of constant pain and fatigue. In these 3 cases both inversion and eversion are limited to approximately the same degree as in the cases with good end-results. In none of the 3 cases is there any lateral bulging of the os calcis.

SUMMARY

The difficult problem of restoring perfect function in the squash-type of fracture with disruption of the subastragalar joint is discussed.

Of the present-day methods of treatment, the Boehler traction method is generally recognized as the most satisfactory. By this method the plane of the joint surfaces may be restored to normal, and the lateral deformity corrected. Uniformly good results may be expected in the majority of cases in which the traction method is used, as based upon the criterion of the recovery of a comfortable, weight-bearing, and functional foot and fitness to resume the accustomed work. The only permanent disability is a limitation of the eversion and inversion of the foot, which constitutes no handicap.

A survey of 22 cases treated by the Boehler method is presented. Nineteen of the patients secured good results and returned to their former occupations.

REFERENCES

1. Boehler, L. The Treatment of Fractures. 4th ed. Translated by Ernest W. Hey-Groves. Baltimore: William Wood & Co., 1935.
2. Carothers, R. Quoted by Stewart, J. E., loc. cit.
3. Ehalt, W. Monatschr. f. Unfallheilk., 1933, 40: 25.
4. Hermann, O. J. New England J. Med., 1930, 202: 705.
5. Jaekle, R. F., and Clark, A. G. Surg., Gynec. & Obst., 1937, 64: 663.
6. Lenormant, C. Presse méd., 1933, 41: 1401.
7. Idem. Helvet. med. acta, 1934, 1: 92.
8. MacAusland, W. R. Surg., Gynec. & Obst., 1936, 63: 506.
9. Murray, G. J. Canadian M. Ass., 1940, 42: 422.
10. Pretty, H. G. J. Canadian M. Ass., 1939, 41: 40.
11. Schofield, R. O. J. Bone & Joint Surg., 1936, 18: 566.
12. Stewart, J. E. South. M. J., 1934, 27: 711.
13. Westheus, H. Zentralbl. f. Chir., 1935, 62: 995.
14. Wilmoth, P. Médecine, 1929, 10: 770.
15. Yoerg, O. W. Lancet, 1939, 59: 530.

PRINCIPLES WHICH GOVERN THE EXTENT OF GASTRIC RESECTION FOR DUODENAL ULCER

VERNE C. HUNT, M.D., F.A.C.S., Los Angeles, California

THE basic principles upon which the philosophy of gastric resection in certain cases of duodenal ulcer is founded are today generally accepted as entirely sound, and partial gastrectomy has attained a status in the treatment of this surgical disease which may be sustained and enhanced by the judicious selection of cases wherein it is justifiably applicable in accordance with its objectives.

As the limitation of indications for surgical intervention in duodenal ulcer has been more closely drawn during recent years, so more frequently have the purposes of an operation been most adequately served through excision of the ulcer. It is true that an ulcer in the anterior wall of the duodenum can be excised by simple conservative procedures and that an ulcer in the posterior wall of the duodenum can often be removed through transduodenal and other relatively conservative operations. However, by this time experience has proved that the incidence of recurrence of ulcer has been high following such conservative operations. Gastric resection provides a method for excision of the ulcer and for the control of gastric acidity and gastric secretion not alone through neutralization and dilution by duodenal or jejunal content but through quantitative reduction of gastric acidity consequent upon the removal of acid-secreting gastric mucosa. It may be stated then that the purposes of gastric resection in certain cases of duodenal ulcer are either excision of the ulcer or quantitative reduction of gastric acidity; but in performing partial gastrectomy both objectives are usually served.

Experience has by this time established the idea that in the bleeding duodenal ulcer, in the penetrating ulcer, and in the ulcer that has recurred following the simple closure of an acute perforation, the purposes of surgical intervention are usually best served through performing partial gastrectomy. By this time everyone is in accord with the idea that recurring hemorrhage from an ulcer usually can be permanently controlled only through excision of the bleeding lesion. The futility of any surgical procedure for the control of bleeding which does not include excision of the bleeding ulcer has been observed so often that one may justifiably say that unless the surgeon is competent and is prepared to excise the ulcer in one way or another, surgical intervention should not be contemplated. Experience has by this time proved that usually a bleeding ulcer can be excised most advantageously through performing partial gastrectomy. Many bleeding duodenal ulcers are situated on the posterior wall of the duodenum, and adequate access to this area to facilitate excision of the ulcer-bearing portion of the duodenum is often gained only after transection of the stomach at some level proximal to the pylorus (Fig. 1).

The penetrating ulcer of the duodenum, particularly the ulcer in the posterior wall in which protective perforation has occurred with subsequent penetration of the pancreas, presents technical problems in its excision, the satisfactory solution of which in many instances is found only through transection of the stomach with removal of the distal portion thereof and the first portion of the duodenum to a level just below the ulcer (Fig. 2). Similar problems are not infrequently encountered when recurrence of an ulcer following simple closure of an acute perforation requires subsequent surgical consideration and the solution of these is likewise at times to be found only through removal of a part of the stomach. It is not to be inferred when partial gastrectomy is performed for duodenal ulcer that the ulcer-bearing area of the duodenum should always be included in the resection. There are instances in which the resection limited distally by the pylorus will suffice and in certain other

Presented at the sectional meeting of the American College of Surgeons, Salt Lake City, Utah, March 26–28, 1941.

Fig. 1. Inclusion of the bleeding ulcer-bearing portion of the duodenum in the hemigastrectomy.

Fig. 2. Inclusion in the hemigastrectomy of that portion of the duodenum with a posterior wall penetrating ulcer.

instances the added hazard of excising a penetrating ulcer in the presence of extensive inflammatory reaction is not justified. However, failure to include an actively bleeding duodenal ulcer within the scope of the resection is a serious compromise of the primary purpose of an operation for this complication.

Failure to control gastric acidity adequately through dilution and neutralization by the conservative operations has provided the impetus for quantitative reduction of gastric acidity and gastric secretion through removal of acid-secreting gastric mucosa by partial gastrectomy. Through partial gastrectomy acid-secreting gastric mucosa in varying amounts may be removed and through restoration of gastrointestinal continuity by gastrojejunal anastomosis the jejunal content becomes available for its additional diluent and neutralizing effect upon gastric acids.

The magnitude of partial gastrectomy for duodenal ulcer as pertains to the amount of stomach which it is advisable to remove is variable and is subject to many factors. The terms partial gastrectomy, subtotal gastrectomy, and gastric resection imply removal of a circumferential portion of the stomach without designation of the amount of stomach which is removed in the resection. Not until qualifying terms are universally adopted to designate the amount of stomach that is removed in the operation of partial gastrectomy can comparative results be determined in terms of the extent of the resection. I have suggested that removal of the pyloric half of the stomach be designated as hemigastrectomy and that the various other magnitudes of gastric resection be designated in terms of thirds, quarters, fifths, et cetera (Fig. 3). Wangensteen has designated the amount of

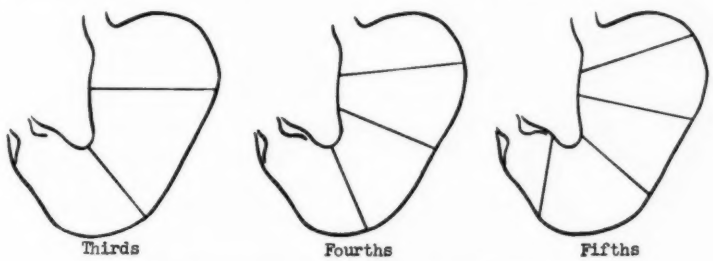


Fig. 3. Designation of the extent of gastric resection.

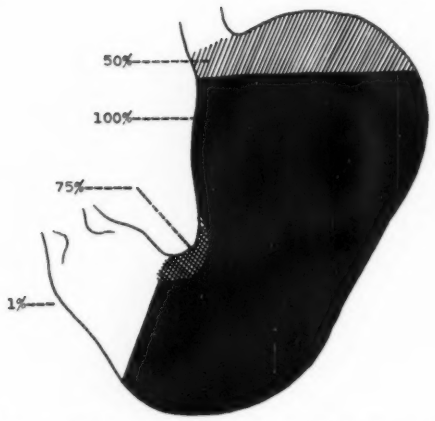


Fig. 4. Distribution of the parietal cells in the gastric glands according to Berger. In the body and fundus of the stomach considerable uniformity exists in the maximum number of parietal cells; in the cross-hatched area at the lesser curvature angle the number of parietal cells in the gastric glands is about 75 per cent of that in the fundus of the stomach; in the lightly shaded area at the cardiac portion of the stomach about 50 per cent, and in the unshaded pyloric antrum about 1 per cent.

stomach removed in terms of the number of square centimeters of serosal surface.

In the quantitative reduction of gastric secretion and gastric acidity by gastric resection two important questions arise: (1) How much shall the gastric secretion and gastric acidity be quantitatively reduced? (2) How much of the stomach shall be removed to provide the desired reduction? These questions, of course, have to do with the problem of recurrent ulcer following partial gastrectomy. It is known that an anastomotic or jejunal ulcer does develop in a small percentage of cases following gastric resection for duodenal ulcer. Heuer's collective review of a large series of cases revealed an incidence of anastomotic or jejunal ulcer following partial gastrectomy in 0.6 to 6 per cent of the cases with an average incidence of 1.9 per cent. All manner of resections and the various methods of restoring gastrointestinal continuity were included in this review, but no analysis of the incidence of recurrent ulcer in relation to the amount of stomach removed or the types of anastomotic procedures which were employed was possible.

There are those whose enthusiasm for quantitative reduction of gastric acidity has led them to extend the operation of gastric resection for duodenal ulcer to the point of establishing constant achlorhydria to histamine stimulation. Wangensteen has said that operations which fail to afford real promise of achlorhydria leave too much to chance and hold out too great a risk of gastrojejunal or recurring ulcer to stamp them as satisfactory operations to be invoked frequently for the surgical relief of ulcer. He likewise has said that to procure achlorhydria with a high degree of regularity it is necessary to sacrifice 66 to 80 per cent of the gastric tissue.

One may not discuss the problems pertaining to the extent of gastric resection without at least brief reference to the structure of the gastric mucosa and the functions of the various constituents of that structure. Three types of glands are present in the stomach of man; and while they are designated as fundic, pyloric, and cardiac, each group is characterized by certain cellular content and secretory product. Bensley recognized only two types of glands: (1) the gastric glands proper which occupy the proximal two-thirds of the stomach and whose function in general is to produce the active elements of gastric secretion, and (2) the pyloric glands which occupy the distal third of the stomach, and whose function is mainly the production of mucus. By this time the individual contribution to gastric secretion of each of the several types of cells comprising the gastric glands is fairly well understood, but the mechanism by which the secretions are produced remains mysterious. While, in general, several different types of cells constitute the gastric glands, certain ones are predominant in each of the three divisions of the stomach. Whatever the mechanism may be by which hydrochloric acid is formed it is generally agreed that the parietal cells in the gastric glands are largely concerned and that the degree of gastric acidity is dependent upon them. They are present in all of the gastric glands, but are most numerous in the glands of the body and fundus of the stomach. Berger, in 1933, showed that in the normal stomach the parietal cells are most numerous with quite consistent uniformity throughout the body of the stomach and that the parietal cells are approximately 75 per cent, 50 per

cent, and 1 per cent as numerous in the gastric glands at the lesser curvature angle, at the cardia and at the pyloric antrum, respectively, as in the glands of the fundus or body of the stomach (Fig. 4).

If one may presume that the preoperative degree of acidity can be reduced proportionately to the amount of parietal cell content of the stomach which is removed by gastric resection, it remains to decide upon what degree of postoperative acidity one wishes to attain in accordance with one's own ideas pertaining to the relationship of the degree of gastric acidity to recurrent gastrojejunal or jejunal ulcer and thereby determine the extent of the gastric resection. If one subscribes to the idea that achlorhydria to histamine stimulation is necessary to provide maximum assurance against recurrent ulcer and that there are no deterrents to a constant achlorhydria, he will of necessity sacrifice 65 to 80 per cent of the gastric mucosa. To sacrifice that amount of gastric structure amounts to practically total loss of gastric function and from a functional standpoint is equivalent to total gastrectomy, for the remaining fragment of stomach no longer serves as a receptacle but serves only as a corridor from the esophagus to the jejunum. It must be carried in mind that constant achlorhydria is not usually maintained without subjective manifestations, and one needs only to retain under observation cases in which three-quarters or four-fifths gastric resections have resulted in constant achlorhydria without recurrence of ulcer to encounter the new problems that have entered the picture as the result of total loss of gastric function. On the other hand, if one can subscribe to the idea that gastric resection of a lesser extent, with preservation of a low degree of acidity will provide reasonable assurance against recurrent anastomotic or jejunal ulcer, satisfactory gastric function can be maintained and the sequelae of constant achlorhydria can be obviated. Or to state the matter otherwise, considerable data have accumulated which strongly support the idea that removal of not more than half of the stomach—hemigastrectomy—provides a reasonable assurance against a subsequent anastomotic or jejunal ulcer, maintains a reduced gastric acidity, and preserves satisfactory gastric function. We also have accumulated data which support the idea that recurrent anastomotic or jejunal ulcer has for the most part in the past developed in those cases in which either pylorectomy, pyloric one-quarter resection or one-third resection has been performed. In my own work I have observed on several occasions such recurrences in cases in which I had previously performed limited gastric resection. On the other hand, I have not observed what might be clinically or roentgenologically suspected as a recurrent anastomotic or jejunal ulcer in which the extent of the gastric resection for duodenal ulcer had been designated as hemigastrectomy.

The degree of gastric acidity is extremely variable, and only through repeated determinations may one approximate the probable average acid curve. From the practical viewpoint, false values are too often obtained upon which the extent of the resection may be predicated and upon which the postoperative results are determined in terms of the degree to which the acids have been quantitatively reduced when the preoperative and the postoperative curves of the gastric acids are plotted after histamine stimulation.

In performing partial gastrectomy for the purpose of quantitatively reducing the gastric acidity one should remain mindful of the fact that dilution and neutralization through gastrojejunal anastomosis operate in conjunction with quantitative reduction in the control of gastric acidity. In other words, the reduction of gastric acidity following gastric resection and gastrojejunal anastomosis is brought about not alone through removal of acid-secreting gastric mucosa, but also through dilution and neutralization by jejunal content, and since diluent and neutralizing material is thereby made available, the quantitative reduction of gastric acidity may be conservative instead of radical to achieve the approximate desired postoperative acid values.

It is my opinion that postoperative achlorhydria not only is not necessary to afford—if not the maximal assurance—at least reasonable assurance against recurrent ulcer but that postoperative achlorhydria is highly undesirable. My own experience with gastric resec-

tion in certain cases of duodenal ulcer has provided me with data which strongly support the thesis that postoperative reduction to approximately one-half of the preoperative degree of acidity provides a reasonable degree of assurance that an anastomotic or jejunal ulcer is a remote possibility. In accordance with this line of reasoning it has been my policy for the most part to confine the magnitude or extent of gastric resection in duodenal ulcer to the pyloric half of the stomach, including the lesser curvature angle of the stomach (hemigastrectomy) and usually the ulcer-bearing portion of the duodenum, resorting to slightly higher resection only in those cases in which the preoperative total acids exceed 100.

It is conceded, even though that has as yet not been my experience, that one may occasionally undershoot the target when performing hemigastrectomy for duodenal ulcer and that an anastomotic or jejunal ulcer may occasionally follow resection of that extent. However, to aim at removal of 75 to 80 per cent of the gastric structure with the sacrifice of most if not all of gastric function in all cases for purposes of obviating the development of an occasional anastomotic or jejunal ulcer hardly seems justified. Such an approach to the problem of the cure of duodenal ulcer is quite analogous to the questionable thesis of total thyroidectomy in the treatment of hyperthyroidism whereby the clinical manifestations and problems of hyperthyroidism are exchanged for those of myxedema.

The results of partial gastrectomy must be analyzed at their full value not only as pertains to the curability of the ulcer, but also in terms of nutritional changes and deficiency states and of the physiological and biochemical processes in the organism as a whole as they are influenced by the magnitude or the extent of the gastric resection. The philosophy of gastric resection in duodenal ulcer has little in common with the principles upon which the rationale of gastric resection and total gastrectomy is founded in the treatment of malignant disease of the stomach. The very nature of the latter disease entirely justifies extensive gastric resection with sacrifice of much and at times all of the gastric structure and the loss of gastric function even though the sequelae of loss of gastric function subsequently become manifested. The evidence is far from conclusive that the curability of benign duodenal ulcer is dependent upon similarly radical gastric resection, and that in order that cure of the ulcer may be achieved the sequelae of major, if not total, loss of gastric function must be accepted.

Through the future universal adoption of one method or another by which the extent of gastric resection may be designated in terms of the amount of stomach which is resected, opportunity may be provided for analysis of the results of the various magnitudes and extents of gastric resection, not only as pertains to the curability of duodenal ulcer but as pertains to the organism as a whole.

THE UTERINE CONTRACTIONS OF LATE PREGNANCY AND THEIR RELATION TO THE DURATION OF LABOR

A Study of 129 Patients with the Lóránd Tocograph

DOUGLAS P. MURPHY, M.D., F.A.C.S., Philadelphia, Pennsylvania

THE present report is one in a series dealing with the contractions of the uterus which occur during pregnancy. The first study concerned simply the magnitude of the contractions which take place during the last 2 months, and the influence of advancing pregnancy upon it (2). The second contribution dealt with the occurrence of contractions early in pregnancy and its relation to the duration of labor (3). The latter investigation indicated that few uteri contract to any extent prior to the ninth lunar month and that patients exhibiting such early activity experience significantly short labors. It also showed that the mere presence of contractions after the beginning of the ninth lunar month is of no assistance in predicting the duration of the labor.

The present investigation, like the first one, deals with the magnitude of the contractions which occur during the ninth and tenth lunar months. It was undertaken, however, in order to find out whether knowledge of this characteristic could be employed as an aid in predicting the kind of activity which would be met with at the time of labor. For this reason it was considered necessary to study few records of many (129) patients rather than many records of a few (5) individuals (2).

MATERIALS AND METHODS

The present observations were made between August 1, 1938, and September 16, 1940, upon patients attending the Maternity Department of the Hospital of the University of Pennsylvania and ones living at the Sheltering Arms Home. All of these women had single pregnancies; all fetal presentations were cephalic, and all deliveries but one were vaginal. No patient exhibited any evidence of cephalopelvic disproportion. The infants weighed between 2,500 and 4,000 grams at birth.

Uterine contractions were recorded with the latest model Lóránd tocograph, shown in Fig. 1 (1). Each patient supplied a single tocographic record made at some time during the 56 days prior to the onset of labor. The recording period in each instance lasted a minimum of 20 minutes. The tocograph supplies a permanent record which makes it possible to measure five characteristics of uterine activity: (a) the hardness or tension of the uterine wall, and the (b) frequency, (c) rhythmicity of occurrence of the intermittent contractions, (d) their strength, and (e) duration.

Uterine tension is a characteristic which it is impossible to measure absolutely by external hysterography. Its relative degree, however, can be expressed in terms of the displacement of the writing pen of the tocograph from its "at rest" position, which occurs as the machine is being placed upon the abdomen of the patient. If the uterus is relatively soft the recording button on the bottom of the tocograph sinks into the abdominal wall and the writing point is not displaced, but if the uterus is hard or tense, the button is forced into the tocograph, in proportion to the tenseness, thus altering the position of the writing pen. The tension is expressed in terms of millimeters of displacement.

The frequency of contractions is expressed as the number per hour.

The rhythmicity of occurrence of contractions is based upon the time interval between the start of one wave and that of the next, and is expressed as the coefficient of variation.

The strength of contraction is measured in terms of the height of the contraction wave and is expressed in millimeters.

From the Gynecean Hospital Institute of Gynecologic Research, Department of Obstetrics and Gynecology, University of Pennsylvania.

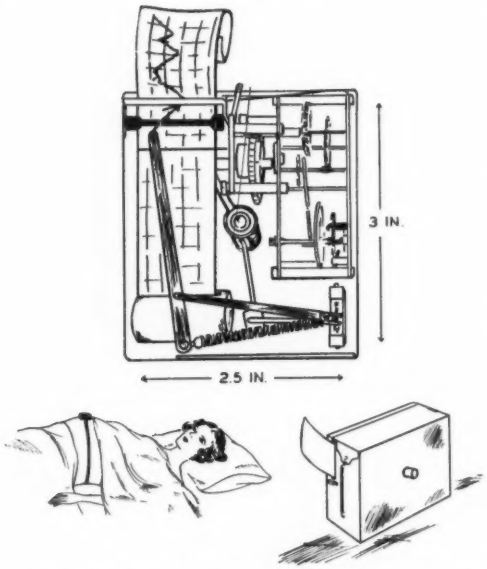


Fig. 1. Latest model Lóránd tocograph, interior and exterior views and in position for recording. Movement of recording button, projecting 0.5 centimeter from bottom of tocograph, is magnified 5 times by writing pen. This instrument is smaller and simpler in construction than model shown in earlier report (2).

The duration of contraction is measured in terms of the length of the contraction wave, and is expressed in seconds.

The magnitude of any characteristic of the uterine contractions of an individual is based upon the measurements of five consecutive waves.

TABLE I.—MEASUREMENTS OF UTERINE TENSION AND CONTRACTIONS DURING 9TH AND 10TH LUNAR MONTHS OF PREGNANCY

	Characteristic				
	Tension*	Contraction wave**			
		Frequency	Rhythm	Height	Duration
Minimum	mm. 0.0	no.-hr. 1.0	c. of v. 0.017	mm. 0.5	seconds 12
Maximum	9.6	84.0	1.017	46.8	516
Mean	1.6±1.9	10.1±13.2	.165±.226	3.4±5.1	80±74

*Based upon 129 tracings.
**Based upon 99 tracings showing contractions.
c. of v.=Coefficient of variation.

Note wide spread between minimum and maximum values and large standard deviation of all means.

TABLE II.—INFLUENCE OF DURATION OF PREGNANCY UPON UTERINE TENSION AND CONTRACTIONS

Duration of pregnancy wks.	Patients					
	No.	Characteristic				
		Mean tension* mm.	Mean contraction wave**			
			Frequency no./hr.	Rhythm c. of v.	Height mm.	Duration seconds
33–34 inc.	3	1.0	14.3	.269	3.6	75
35–36 inc.	12	1.1	4.4	.111	2.8	80
37–38 inc.	36	1.2	10.2	.126	1.2	31
39–40 inc.	78	2.0	10.8	.187	4.8	101

*Based upon 129 tracings.
**Based upon 99 tracings showing contractions.
c. of v.=Coefficient of variation.

As pregnancy advances note: (a) progressive increase in tension, (b) stabilization of the frequency of contractions during last month, (c) unusual increase in the height (strength) and duration of the contraction waves during the 39–40 week period, and low values for these measurements during the 37–38 week period.

RESULTS

Of 129 patients, 71 were white, 58 colored; 52 were primigravidas, 87 multigravidas.

Distribution of measurable characteristics. Tension was measured in 129 tracings, the height, duration, and frequency of contraction waves in the 99 tracings in which waves were observed, and rhythm only in those tracings which recorded three or more contractions.

Summary of all measurements. Minimum, maximum, and mean values of tension and

TABLE III.—INFLUENCE OF DURATION OF PREGNANCY UPON DISTRIBUTION OF PATIENTS HAVING NO UTERINE CONTRACTIONS

Duration of pregnancy wks.	Patients			
	No.	%	With no contractions	
			No.	%
33–34 inc.	3	2.3	0	0.0
35–36 inc.	12	9.3	4	12.9
37–38 inc.	36	27.9	18	58.1
39–40 inc.	78	60.5	9	29.0
Total	129	100.0	31	100.0

Note that an absence of contractions was observed most frequently in tracings secured during the 37–38 week period, where contractions of small magnitude were observed (Figure 2).

TABLE IV.—INFLUENCE OF PARITY UPON UTERINE TENSION AND CONTRACTIONS

Parity	Patients						
	No.	Characteristic					Mean duration of labor hrs.
		Mean tension mm.	Mean contraction wave*				
			Frequency no./hr.	Rhythm c. of v.	Height mm.	Duration seconds	
Primiparas	42	2.0± 2.0	20.2± 18.8	.310± .217	3.2± 2.1	103± 95	16.0± 10.1
Multiparas	87	1.4± 2.0	10.3± 13.0	.290± .238	4.5± 3.0	106± 69	8.9± 7.4

*Measurements of primiparas based upon 34 tracings showing contractions.
Measurements of multiparas based upon 64 tracings showing contractions.
c. of v.=coefficient of variation.

Note: (a) difference in mean duration of labor, (b) the lower frequency of contractions, and their greater rhythmicity, strength and duration in the multiparas.

contractions appear in Table I. These data attest to the wide individual variation of all measurements.

Influence of duration of pregnancy upon uterine tension and contractions. The mean values of tension and of all characteristics of the contractions of the contraction waves are shown in Table II, arranged according to the duration of pregnancy at the time that they were recorded. Tension increased progressively as pregnancy advanced. The frequency of contractions appeared to become stabilized during the last month, although there was no significant improvement in rhythmicity.

The height and duration of the contraction waves were greatest during the 2 weeks immediately before labor, but were unusually small during the 37 to 38 week period.

Influence of duration of pregnancy upon distribution of tracings registering no uterine contractions. Thirty-one tracings registered no contractions. Table III records their distribution according to the time in pregnancy that they were secured. Although the majority of all tracings were made during the 39 to 40 week period, tracings showing no contractions appeared most often in the preceding two week period. It is significant that the presence of low grade contractions (Table II) was ob-

TABLE V.— INFLUENCE OF UTERINE WALL TENSION UPON DURATION OF LABOR

Tension in millimeters	Patients	
	No.	Mean duration of labor in hours
Reported	129	11.2± 9.0
0.0*	63	11.5± 8.7
0.1–4.9	52	10.6± 7.6
5.0–9.9	14	12.2± 13.5

*No increase in tension observed.

Note that the highest degree of tension was followed by the longest labors.

TABLE VI.—INFLUENCE OF FREQUENCY OF CONTRACTIONS UPON DURATION OF LABOR

Contractions per hour	Patients	
	No.	Mean duration of labor in hours
Reported	129	11.2± 9.0
0.0*	31	10.3± 6.8
0.1–9.9	56	10.3± 9.8
10.0 plus	42	13.2± 8.8

*No contractions recorded.

Note that the short labors were associated with an absence of contractions, or with ones of low frequency.

TABLE VII.—INFLUENCE OF RHYTHMICITY OF CONTRACTIONS UPON DURATION OF LABOR

Coefficient of variation	Patients	
	No.	Mean duration of labor in hours
Reported	129	11.2± 9.0
0.000*	57	9.7± 5.5
0.001–0.299	45	11.1± 10.1
0.300–0.599	19	14.0± 10.5
0.600 plus	8	16.2± 7.2

*Number of contractions insufficient for computing coefficient of variation.

Note that the shortest labors were associated with the lowest coefficient of variation.

TABLE VIII.—INFLUENCE OF STRENGTH OF CONTRACTIONS UPON DURATION OF LABOR

Wave height in millimeters	Patients	
	No.	Mean duration of labor in hours
Reported	129	11.2± 9.0
0.0*	31	10.3± 6.9
0.1– 4.9	64	11.8± 8.6
5.0– 9.9	31	11.8± 17.9
10.0–14.9	3	3.9± 15.3

*No contractions recorded.

Note shortness of labors in patients experiencing no contractions, and the very short labors in those having the strongest contractions.

TABLE IX.—INFLUENCE OF DURATION OF CONTRACTIONS UPON DURATION OF LABOR

Duration of contraction in seconds	Patients	
	No.	Mean duration of labor in hours
Reported	129	11.2±9.0
0.0*	31	10.3±6.9
0.1– 29.9	7	17.3±9.6
30.0– 59.9	20	11.2±6.6
60.0– 89.9	23	13.6±8.2
90.0–119.9	18	9.6±8.8
120.0 plus	30	9.9±8.3

*No contractions recorded.

Note shortening of labors as the duration of contractions increases.

served at the same time. Perhaps this drop in activity may have an endocrine basis.

Influence of parity upon contractions. The magnitude of the contractions of the primiparas (primigravidas) is compared with that of the multiparas in Table IV. The latter exhibited shorter labors which were preceded by: (a) lower tension, (b) less frequent contractions; these were (c) more rhythmic, (d) stronger and (e) longer than those of the primiparas. The most obvious difference was in contraction frequency.

Influence of individual contraction characteristics upon duration of labor. The influence of the contraction characteristics, considered separately, upon the duration of labor appears in Tables V to IX. The standard deviations of all measurements are large, indicating the wide variability in individual characteristics. The data are such that no significant differences are observed between classes in any one table. In spite of this fact certain trends appear: The shortest labors occurred under the following conditions: (a) a low uterine tension, and (b) when the contractions were infrequent, rhythmic, strong, and of long duration.

Contraction measurements of patients having different length labors. Contraction measurements of patients having labors of less than 8 hours are compared with those of women who had labors lasting more than 16 hours, in Table X. The shorter labors were preceded by (a) a lower contraction frequency, (b) greater

TABLE X.—MEASUREMENTS OF UTERINE TENSION AND CONTRACTIONS IN RELATION TO DURATION OF LABOR

Labors	Patients					
	No.	Characteristic				
		Mean tension mm.	Mean contraction wave*			
			Frequency no./hr.	Rhythm c. of v.	Height mm.	Duration seconds
All	129	1.6± 1.9	10.1± 13.2	.165± .226	3.4± 5.1	80± 74
Under 8 hours	55	2.0± 2.3	9.5± 8.7	.275± .202	4.3± 3.0	119± 239
Over 16 hours	23	1.8± 1.8	12.7± 19.9	.308± .242	3.8± 2.2	88± 51

*Measurements of "under 8 hours" group based upon 42 tracings showing contractions.
*Measurements of "over 16 hours" group based upon 19 tracings showing contractions.
c. of v.=Coefficient of variation.

Mean values of the contraction measurements of patients having labors of more than 16 hours compared with those having labors of less than 8 hours' duration. Note that the patients having shorter labors experience: (a) a low contraction frequency, (b) greater rhythmicity in the occurrence of contractions, (c) stronger and (d) longer contractions than those having longer labors.

rhythmicity, (c) stronger and (d) longer contractions, and (e) greater tension than were the longer labors.

OBSERVATIONS

The patients supplying the present observations fall into two groups: those who experienced contractions and those who did not. The latter individuals had shorter labors than the average. It would follow from this that the absence of contractions is no sign that the labor will be long.

The contractions exhibited a wide variation in their measurements from individual to individual. This was so great that it would seem difficult to predict the length of any given patient's labor on the basis of a single tocographic record. In spite of this variability there did exist a relation between the nature of the uterine motility during the ninth and tenth months of pregnancy and the length of labor.

Tension was found to have no value in predicting the duration of the labor, whereas knowledge of the contractions was a help. The short labor was usually preceded by contractions which were found to be especially infrequent, rhythmic, long and strong.

Certain other features of the contractions, which do not lend themselves readily to statistical treatment, also indicate that a satisfactory type of labor can be expected. Contractions which rise slowly to a maximum and fall away at the same rate, almost regardless of their strength, prognosticate a more efficient kind of activity during labor than ones which rise and fall quickly. This may be only another way of saying that a long contraction is better than a short one. Certain patients present a contraction pattern of such a kind that it is possible to superimpose one wave and its following valley upon an adjacent one. Such patients may be said to exhibit a nearly perfect rhythmicity in respect to all characteristics of their contraction waves, e. g., size, shape, duration, frequency, and rhythmicity. These women experience short labors. The short labor can be predicted more upon the quality of the contractions than upon their size. Rhythmicity in all characteristics of the contraction appears to be the ideal to be attained if the quality of the labor is to be optimum.

SUMMARY AND CONCLUSIONS

1. The uterine motility of 129 patients was recorded with a Lóránd tocograph during the ninth and tenth lunar months of pregnancy.

2. Measurements of tension, and of frequency, rhythmicity of occurrence, strength and duration of the contractions were correlated with: (a) time of recording, (b) parity, and (c) duration of labor.

3. Measurements of all characteristics of motility exhibited wide individual variations.

4. Advancing pregnancy was associated with: (a) a progressive increase in tension, (b) a tendency for the frequency of contractions to become stabilized during the last month, (c) absence of contractions, and ones of unusually small magnitude during the 37 to 38 week period, (d) exceptionally long, strong contractions during the 39 to 40 week period.

5. Multigravidas and individuals experiencing short labors exhibited contractions during late pregnancy which were: less frequent, more rhythmic in occurrence, stronger and longer in duration than did primigravidas and individuals who had longer labors.

6. From these observations two conclusions seem justified: (a) The duration of labor of a given individual cannot necessarily be predicted from an examination of a single tocographic record made at random during the last two lunar months of pregnancy. (b) In general short labors are preceded by a uterine motility which differs from that experienced by individuals who have longer labors.

REFERENCES

1. Lóránd, S. (Loewi). Monatschr. f. Geburtsh. u. Gynaek., 1936, 103: 137–145.
2. Murphy, D. P. Surg., Gynec. & Obst., 1940, 70: 129–135.
3. Ibid., 1941, 73: 498–501.

THE INTRAVENOUS USE OF SYNTHETIC VITAMIN K_1

ARNOLD M. SELIGMAN, M.D., ALFRED HURWITZ, M.D., HOWARD A. FRANK, M.D., and WILLIAM ANTHONY DAVIS, M.D., M.S., Boston, Massachusetts

THE clinical value of vitamin K is well established. Various substances with vitamin K activity have served to relieve the bleeding tendency associated with prothrombin deficiency in obstructive jaundice, hemorrhagic disease of the newborn, various disorders of the liver, and of the intestinal and biliary tracts.

Since the presence of bile in the intestinal tract is required for the absorption of the vitamin, oral therapy, in cases of complete biliary obstruction or fistula, necessitates the giving of bile salts. Nausea and vomiting, often increased by the ingestion of bile salts, make oral administration uncertain and sometimes impossible.

A method of administering synthetic vitamin K_1 (2-methyl-3-phytyl-1, 4-naphthoquinone—see Fieser, 6) intravenously has been described by three of us (10). The rapidity and prolonged duration of action of single doses of vitamin K_1, when administered intravenously, exceed those reported by other investigators using drugs with vitamin K activity by oral, intramuscular and intravenous routes. (2, 3, 11, 19, 20, 22). This paper presents the results of further studies of the intravenous use of synthetic vitamin K_1. It also includes certain data on the effects of the intravenous administration of 2-methyl-1, 4-naphthoquinone and of a water soluble sulfuric ester of 2-methyl-1, 4-naphthohydroquinone.[1]

METHOD

Through the courtesy of Professor Louis F. Fieser, synthetic vitamin K_1 was obtained for this study. This substance, which is an oil at room temperature, was given intravenously in a colloidal suspension, prepared by dissolving 10 milligrams of the vitamin in 3 cubic centimeters of ethanol and introducing the solution slowly under the surface of 1 liter of a 10 per cent solution of glucose in distilled water, while this was being constantly agitated. The suspension was then autoclaved for 20 minutes at 120 degrees C. The product was slightly opalescent. No change in appearance was noted in ampuls of the suspension which had been stored for 5 months, and the material was found to have retained its activity during this time. Because quinones are altered by sunlight, the solutions were stored in the dark. No untoward reaction followed the use of this material when given intravenously. In a case in which it was not possible to evaluate the effectiveness of the drug, no local reaction followed the administration of the colloidal suspension by clysis. 2-Methyl-1, 4-naphthoquinone was prepared for intravenous use in the same way and was found to be slightly more soluble. Doses of 10 to 20 milligrams of the sodium salt of the sulfuric ester of 2-methyl-1, 4-naphthohydroquinone are readily soluble in 1 cubic centimeter of water.[2]

Prothrombin times were determined by the method of Quick (13). The range for normal adults was 14 to 17.5 seconds when the thromboplastin plasma mixture was brought to 37 degrees C. before the addition of calcium chloride.

RESULTS

Obstructive Jaundice

The results in obstructive jaundice are shown in the following case histories.

H. R. B., No. P.B.B.H. s62750, a 79 year old man, entered the hospital because of recurrent vomiting and jaundice. He had been well until 8 months before entry when he began to vomit with increasing frequency, although he had no nausea. Two weeks before his entrance into the hospital he became jaundiced; his stools became clay colored, and his urine became dark.

From the Surgical Service, Beth Israel Hospital and the Medical Service, Peter Bent Brigham Hospital.

Presented in part before the Harvard Medical Society on April 6, 1940, at the Peter Bent Brigham Hospital, New England Journal of Medicine, 223: 117, 1940.

This study was aided by a grant from the Proctor Fund Department of Medicine, Harvard Medical School.

[1]Synthesized (8) and kindly supplied by Professor Louis F. Fieser.

[2]For stability an equal weight of sodium bicarbonate was dissolved in the solution.

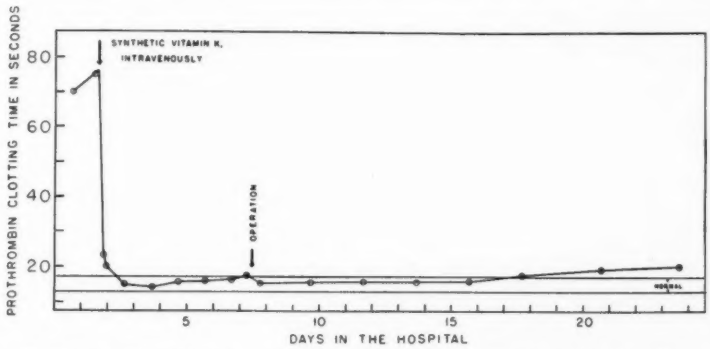


Chart 1. Prothrombin time determinations in case H. R. B., obstructive jaundice.

Examination revealed emaciation and jaundice. There was slight tenderness in the right upper quadrant of the abdomen. The liver dulness extended downward from the fifth interspace, and the edge could be palpated 5 centimeters below the costal margin in the midclavicular line. Laboratory data included: white blood cells, 8,600, with normal differential; stools, clay colored, guaiac positive; urine contained bile; vomitus, dark guaiac positive; icterus index, 125. Bleeding time was 5 minutes; clotting time 5 minutes, 30 seconds; prothrombin time, 70 seconds. There were marked ecchymoses about the needle puncture wounds. The patient was given 10 milligrams of vitamin K_1 intravenously 24 hours after admission. Laparotomy was performed on the seventh hospital day. The liver was found to be studded with metastatic carcinoma arising in the head of the pancreas, and no palliative procedure was possible. There was no unusual bleeding during the operation.

Following laparotomy, the patient continued to vomit. He received all nourishment parenterally. He discharged much bile-stained fluid through the abdominal wound, and the stools remained clay colored. He showed no tendency to bleed. His course was progressively downhill and he died on the twenty-sixth hospital day. Autopsy revealed carcinoma of the head of the pancreas with metastases to liver and mesentery, with obstruction of the common bile duct.

This patient with obstructive jaundice of at least 2 weeks' duration entered with an abnormal prothrombin level which was associated with a bleeding tendency. A single dose of vitamin K_1 produced a marked drop in prothrombin time in 4 hours and a return to normal within 16 hours. He underwent operation 6 days later, with a normal prothrombin level. There was no abnormal bleeding. Although the operation failed to relieve the biliary obstruction, his prothrombin level remained within normal limits for 2 weeks without additional vitamin K. The prothrombin time determinations are recorded in Chart 1.

E. F. C., No. P.B.B.H. s63362, a 52 year old man, entered the hospital because of progressive weight loss and jaundice. During the previous 7 years he had consumed large quantities of alcohol. Six weeks before entry he began to lose his appetite, and 3 weeks before entry he became jaundiced; his stool became clay colored, his urine dark. His nose bled several times during the weeks before admission.

Examination revealed an obese white man with yellow, excoriated skin and icteric sclerae. The abdomen was large. The liver dulness extended down from the fifth interspace and a firm, smooth, non-tender liver could be felt 4 fingers' breadths below the costal margin. The area of splenic dulness was enlarged. Laboratory data included: white blood cells 6,650, with normal differential; icterus index, 74; serum protein 6.0 grams; albumin, 2.3 grams; globulin, 3.7 grams; bromsulphthalein test showed 60 per cent retention at 30 minutes; urine contained albumin and bile; stools were clay colored without bile; bleeding time, 2½ minutes; clotting time, 2 minutes; prothrombin time, 48 seconds.

In the hospital epistaxis continued. There were ecchymoses about the needle puncture wounds. One half-milligram of vitamin K_1 was given intravenously. The nosebleeds stopped. Two days before operation 10 milligrams of vitamin K_1 were given intravenously. Operation, performed on the nineteenth hospital day, revealed marked hepatitis, cirrhosis, and many large and small carcinomatous nodules in the liver. No palliative procedure was possible. There was no abnormal bleeding at operation, and the wound healed well. The postoperative course was one of progressive weakness with jaundice. The urine continued to contain bile. There was no evidence of bile in the stools at any time. There was no recurrence of bleeding and no further vitamin K was given. On the thirty-fifth hospital day he was discharged to a convalescent home.

Chart 3

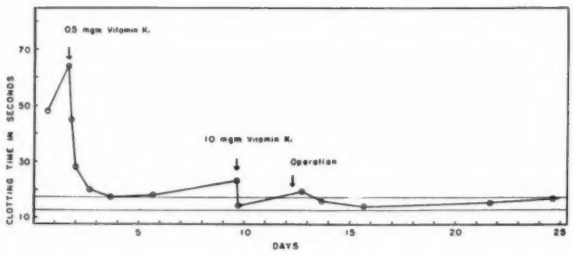


Chart 2

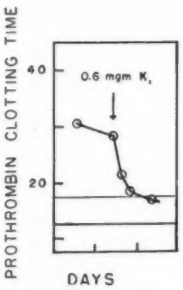


Chart 4

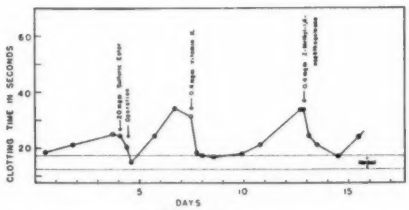


Chart 5

Chart 2. Prothrombin time determinations in case E. F. C., obstructive jaundice.

Chart 3. Prothrombin time determinations in case A. K., obstructive jaundice.

Chart 4. Prothrombin time determinations in case I. B., obstructive jaundice.

Chart 5. Prothrombin time determinations in case S. C., obstructive jaundice.

This patient with obstructive jaundice of at least 3 weeks' duration entered the hospital with an abnormal prothrombin level. The response to 0.5 milligram of vitamin K_1 intravenously is shown in Chart 2. The prothrombin level reached normal 2 days after injection but rose again to 24 seconds in 5 days. The slow response to this dose may have been due in part to the cirrhosis and hepatitis noted at laparotomy.

Following a 10 milligram dose of vitamin K_1 the prothrombin level returned to normal and remained so for at least 15 days, despite the fact that the patient underwent an operation which did not relieve the biliary obstruction.

A. K., No. P.B.B.H. m57109, a 70 year old woman, entered because of nausea and jaundice. Two years before entry she had had painless jaundice, nausea, and fatigue, which subsided after about a month. Except for occasional bouts of nausea, she had been well until 6 weeks before entry when she had a shaking chill followed by vomiting and diarrhea. She developed jaundice, had tarry stools, and vomited large quantities of coffee ground material. Two days before entry she again had chills with a fever of 102 degrees F., and had several dark bowel movements.

Examination revealed an elderly icteric woman vomiting frequently. There were a few râles at the lung bases and a soft systolic apical murmur. The liver could be percussed 1 finger's breadth below the costal margin. The gall bladder was not felt. Laboratory data included: hemoglobin, 55 per cent; red blood cells, 3,300,000; white blood cells, 23,600 with 93 per cent neutrophiles; urine contained bile, albumin, acetone, diacetic acid, occasional red blood cell, white blood cell, and hyaline casts. Stools could not be obtained. The vomitus was black, benzidine positive. The icterus index was 80. The prothrombin time was 118 seconds. Ten milligrams of vitamin K_1 was given intravenously. At that time there were ecchymoses about the needle puncture wounds and the patient was vomiting bloody material. She continued to vomit grossly bloody fluid. Her course was progressively downhill and she died 40 hours after entry.

Postmortem examination was performed with the following findings: carcinoma of the ampulla of Vater with obstruction of the common bile duct;

suppurative cholangitis; generalized icterus; biliary hemorrhage and gastrointestinal hemorrhage.

This woman entered the hospital with obstructive jaundice, bleeding, and marked prothrombin deficiency. Although she was moribund on admission and died 40 hours thereafter, the prothrombin time dropped from 118 seconds to 18.5 seconds within 4 hours after a single 10 milligram dose of vitamin K_1 was given. The prothrombin determinations are recorded in Chart 3.

I. B., No. P.B.B.H. s63751, a 70 year old woman, entered the hospital because of jaundice and itching. She had been well until 5 months before entry when she began to lose weight. One month before entry she became jaundiced, had orange urine, and passed pale stools.

Examination revealed jaundice, bleeding excoriations of the skin and liver edge palpable 1 finger's breadth below the costal margin. Laboratory data included: white blood cells 7,600 with 66 per cent neutrophiles; urine contained bile and occasional red blood cell; stools, clay colored, guaiac positive; icterus index, 62; non-protein nitrogen 42 milligrams per cent; total serum protein, 6.9 grams. The prothrombin time was 30 seconds. She was given 0.6 milligram of vitamin K_1 intravenously on her third hospital day. Two days later a laparotomy was performed which was attended by no unusual bleeding. The head of the pancreas was found to be markedly enlarged, distorting the duodenum. Cholecystgastrostomy was done. Following the operation the icterus index dropped, the urine became pale, and bile appeared in the stools. She was discharged on the sixteenth hospital day.

This patient with obstructive jaundice of at least 1 month's duration entered with an abnormal prothrombin time. The prothrombin deficiency was corrected within 16 hours by a single dose of only 0.6 milligram of vitamin K_1. The prothrombin time determinations are recorded in Chart 4. The autoclaved colloidal suspension used in this case had been stored in sealed glass ampuls in the dark, at room temperature, for 5 months before use.

S. C., No. B.I.H. 51382, a 45 year old woman who had had cholecystectomy for cholelithiasis without jaundice 5 months earlier, entered, stating that she had drained large amounts of bile from her wound for a month after operation. After the drainage stopped, she developed increasing jaundice. The stools had remained clay colored in the postoperative period and bile appeared in the urine with the development of jaundice.

Examination disclosed deep icterus and a smooth, firm, non-tender liver, palpable 4 fingers' breadth below the costal margin. The urine contained large amounts of bile; stool, pale; icterus index, 140; cholesterol, 320; cholesterol esters, 178; non-protein nitrogen, 27; prothrombin time, 19 seconds.

Because of a slowly rising prothrombin time a water soluble sulfuric ester of 2-methyl-1, 4-naphthohydroquinone was given intravenously before operation. At operation the common duct was found to be completely transected and the liver bile was colorless. Anastomosis about a T-tube was accomplished. There was no unusual bleeding during or after the operation. The convalescence was satisfactory and the T-tube drained bile which became golden-brown in color. The icterus index fell; bile disappeared from the urine, and the stools became brown. Because the prothrombin time rose after operation the effect of a minimal dose of vitamin K_1 was investigated and the effect was compared with that of the same small dose of 2-methyl-1, 4-naphthoquinone. The patient was discharged on the seventeenth postoperative day with T-tube remaining in place, draining bile.

This patient with postcholecystectomy jaundice which followed the spontaneous closure of a biliary fistula showed increasing hypoprothrombinemia early in the second postoperative period after reconstruction of the common duct, despite the return of bile to the intestinal tract. Four tenths milligram of vitamin K_1 caused a reduction in the prothrombin time from 31 seconds to 18.5 seconds within 6 hours and maintained the level near normal limits for 2 days. On the other hand, this same dose of 2-methyl-1, 4-naphthoquinone, administered in the same way on a later occasion, required 36 hours for a reduction in clotting time to normal, and the effect was shorter in duration. This was noted in spite of the fact that the patient was putting more bile into her intestinal tract and thus perhaps was absorbing additional vitamin K from her food during the latter period of observation. The effect of a large dose of the water soluble ester of 2-methyl-1, 4-naphthohydroquinone, given before operation was found to be short. The prothrombin time determinations are recorded in Chart 5. The case exemplifies the possibility of postoperative fall in blood prothrombin despite the return of bile to the intestinal tract. This may be related to the failure of production of bile acids by the liver immediately after release of biliary obstruction (15, 16).

The intravenous injection of synthetic vitamin K_1 was effective in the treatment of prothrombin deficiency of obstructive jaundice.

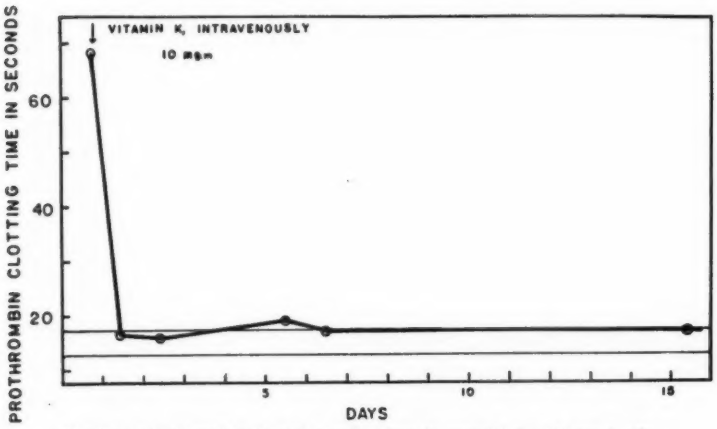


Chart 6. Prothrombin time determinations in case M. L., biliary fistula.

Marked drops in prothrombin time were observed within 4 hours after injection, and normal levels were reached within 10 to 16 hours. A 10 milligram dose resulted in the maintenance of a normal prothrombin level for as long as 15 days of unrelieved biliary obstruction. A half milligram dose showed a distinct response which was of short duration. No difficulty occurred in the preparation of these patients for operation and no unusual bleeding accompanied or followed the surgical procedures.

In one case, a small dose (0.5 milligram) of vitamin K_1 gave a better effect than the same dose of 2-methyl-1, 4-naphthoquinone. In this same patient the effect of a large dose (20 milligrams) of a water soluble ester was noted to be shorter than that of the small doses of the quinones. This case study also emphasized the necessity of watching the prothrombin level in the immediate postoperative period, even though the flow of bile has been returned to the intestinal tract.

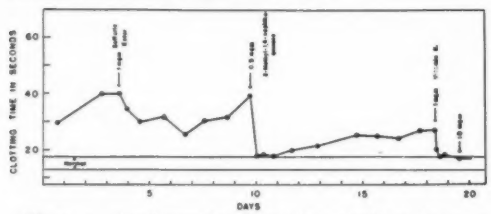


Chart 7. Prothrombin time determinations in case H. M., biliary fistula.

Despite the more frequent occurrence of obstructive jaundice due to calculus, significant prothrombin deficiency was found more often in cases of malignant biliary obstruction.

Biliary Fistula

The results in biliary fistula are shown in the following cases.

M. L., No. M.G.H. 175730[1], a 23 year old female underwent cholecystectomy for recurrent attacks of biliary colic of 2 years' duration. At operation chronic cholecystitis with multiple stones was found. After operation bile leakage into the subhepatic space occurred. After this was drained, a total biliary fistula developed. The patient was very ill and vomited frequently. The blood prothrombin level fell markedly within 10 days despite persistent attempts to feed the patient's own bile, bile salts, and vitamin K by mouth and through a stomach tube. The patient was transfused repeatedly. Jejunostomy was done for feeding purposes and at this time bleeding was noted in the peritoneal cavity. In the subsequent 8 months the patient was given her own bile, supplementary bile, and vitamin K preparations through the jejunostomy or by mouth. This period included an unsuccessful attempt to reconstruct the biliary tract.

The present admission occurred 4 months after the latter operation, throughout which period the patient stated that she had continued to take her own bile, as well as commercially available vitamin K preparations, by mouth. There is some question, however, as to how faithfully she had done so. She re-entered the hospital because of the spontaneous development

[1]Acknowledgment is made to the Massachusetts General Hospital for permission to study this case.

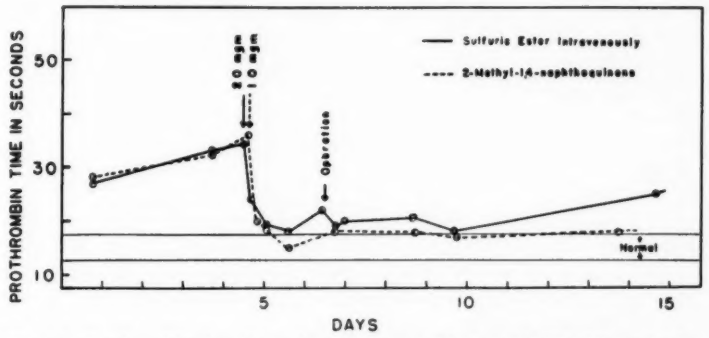


Chart 8. Prothrombin time determinations in cases M. G. and H. M., biliary fistulas.

of numerous large ecchymotic areas over the extremities. On admission she was noted to have in addition to the ecchymoses, oozing gums and a swollen knee containing fluid. The neck was noted to be stiff and lumbar puncture disclosed blood in the spinal fluid. Shortly after admission, uterine bleeding started and puncture wounds were noted to bleed protractedly. Her prothrombin time was 68 seconds. Ten milligrams of vitamin K_1 were given intravenously, and her prothrombin level returned to normal within 10 hours. The clinical evidences of bleeding ceased. The patient proceeded to recover from the effects of the subarachnoid hemorrhage. She continued to get bile, bile salts, and vitamin K preparations by mouth and compounds with vitamin K activity parenterally. She later underwent an operative correction of her biliary fistula.

This patient with biliary fistula developed prothrombin deficiency on several occasions despite the attempt to return the patient's own bile continuously, by mouth or by jejunostomy, and despite the frequent additional administration of bile acids and crude extracts with vitamin K activity into the gastrointestinal tract. Persistent nausea and vomiting required the formation of a feeding jejunostomy. Intravenously administered synthetic vitamin K_1 on one occasion resulted in the prompt restoration of a normal prothrombin level. The duration of effect of this dose cannot be estimated because of the continuation of other forms of vitamin K therapy. The prothrombin determinations are recorded in Chart 6.

H. M., No. B.I.H. 38778, a 60 year old white female, entered complaining of recurrent attacks of upper abdominal pain with feverishness and weakness during the preceding 6 weeks. Cholecystography disclosed numerous stones and cholecystectomy was done. After operation a total biliary fistula developed. The patient vomited repeatedly. Wound rupture occurred and was repaired. She continued to drain large amounts of bile for 3 months, during which time her stools remained clay colored or occasionally pale tan. Her appetite remained poor; she suffered almost constant nausea and repeated vomiting, and she lost much weight. The prothrombin time over 6 weeks gradually rose to 36 seconds and 10 milligrams of 2-methyl-1, 4-naphthoquinone were given (see Chart 8). A second laparotomy revealed complete transection of the common duct. The duct was reconstructed about a catheter through which the patient drained bile externally.

After operation persistent nausea prevented adequate nutrition, and transfusions of whole blood and of plasma were given to correct hypoproteinemia. By the second postoperative week the prothrombin time had risen to 40 seconds. In the course of the following 2 weeks, 3 antihemorrhagic substances were given in minimal doses to compare their effects (see Chart 7). In the third postoperative week the amount of biliary drainage diminished, and the patient was able to tolerate clamping of the catheter without discomfort and without rise in icterus index. Occasional stools became tan in color although the mercuric chloride test for bile remained negative. Positive guaiac reactions were noted in the stools. On the twenty-fourth postoperative day, profuse hemorrhage through the common duct catheter occurred; the stools became tarry and the patient went into shock. She was given intravenous glucose in saline, whole blood and 10 milligrams of vitamin K_1. The patient recovered rapidly. The catheter, which had become filled with blood clot, was removed. The bleeding stopped; the amount of bile draining from the fistula steadily diminished and the fistula closed spontaneously. No icterus developed. The stools became dark brown, guaiac negative, and gave positive mercuric chloride tests for bile. She was discharged, well, on the fifty-first postoperative day.

Hypoprothrombinemia in this case was caused by a complete biliary fistula secondary

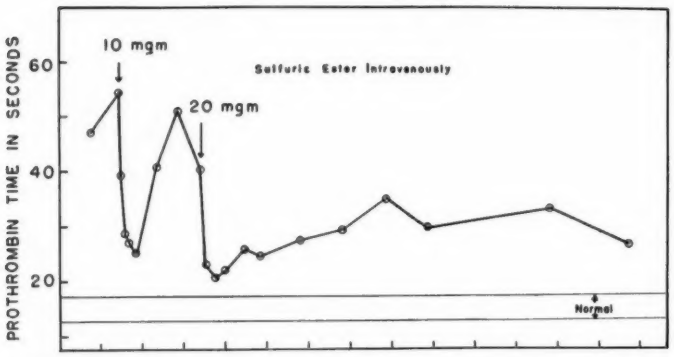


Chart 9. Prothrombin time determinations in case M. G., biliary fistula.

to transection of the common duct. At one period in the course of the patient's illness, 10 milligrams of 2-methyl-1, 4-naphthoquinone were given and the course of the prothrombin times shown in Chart 8 may be compared with the effect of a 20 milligram dose of the water soluble sulfuric ester of 2-methyl-1, 4-naphthohydroquinone given to a patient with obstructive jaundice which became converted to a biliary fistula (M. G.). This case afforded an opportunity to compare the efficacy of several antihemorrhagic substances. Small doses were used in order to bring out their differences. Chart 7 shows the effect of 1 milligram of a water soluble sulfuric ester of 2-methyl-1, 4-naphthohydroquinone, of 0.5 milligram of a colloidal suspension of 2-methyl-1, 4-naphthoquinone, and of 1 milligram of vitamin K_1, given after the second laparotomy. The chart shows the poor effect of the water soluble ester and the marked drop in prothrombin clotting time which reached normal within 24 hours after injection of 0.5 milligram of 2-methyl-1, 4-naphthoquinone. The level remained near normal limits for about 24 hours and then gradually rose again. This may be contrasted with the longer effect of the larger dose given on the previous occasion. The curve of action of 1 milligram of vitamin K_1 was not followed to completion in this case because of the serious bleeding from the common duct which prompted the surgeon to give the patient an additional 10 milligrams of the vitamin. The bleeding stopped after the catheter was removed, and was probably due to ulceration of the common duct by the catheter.

M. G., No. B.I.H. 22209, a 65 year old white female, entered complaining of right upper quadrant pain associated with nausea and fever of 5 hours' duration. She had had similar attacks in the past year and a half. Examination revealed evidence of marked weight loss, sallow skin, tenderness, spasm, and a palpable mass in the right subcostal region. The icterus index was 4; white blood cells, 24,000, and temperature 102 degrees F. Laparotomy was performed, and a pus filled gall bladder containing many stones was removed. After operation the patient developed bilateral pneumonia. Sulfapyridine therapy was instituted for 4 days with good results. Throughout the postoperative period, biliary drainage from the wound was profuse, and the stools were clay colored. The mercuric chloride test for bile in the stools was consistently negative after the fifth postoperative day. The prothrombin clotting time on the sixth day following operation was 47 seconds. The patient was treated on two occasions with a water soluble sulfuric ester of 2-methyl-1, 4-naphthohydroquinone.

On the twenty-fourth postoperative day, drainage ceased and the patient became increasingly jaundiced. Icterus index rose to 37 and clay colored stools persisted. The prothrombin clotting time had gradually increased and on the twenty-fourth day was 34 seconds. She was again treated with the water soluble ester. Two days later an exploratory laparotomy was performed, but the common duct could not be found. She received a blood transfusion. Bilateral pneumonia recurred and again responded to sulfapyridine by the fourth postoperative day. After operation she developed a biliary fistula and clay colored stools which persisted until the fourteenth postoperative day, when biliary drainage ceased and her stools became brown. Four days later she was discharged with an icterus index of 3 and prothrombin clotting time of 20 seconds. The patient was again seen in the out-patient department 2 months

later because of epigastric pain, vomiting, and weakness, and was found to be jaundiced. She refused hospitalization and it was learned that she had died at home on the following day.

This patient with a complete biliary fistula following cholecystectomy was found to have a prolonged prothrombin clotting time on the sixth postoperative day. Both a 10 milligram and a 20 milligram dose of a water soluble sulfuric ester of 2-methyl-1, 4-naphthohydroquinone were given intravenously with the effects shown in Chart 9. Although the drops in prothrombin time were rapid, at no time did they reach normal, and the duration of effect was short. The coexistent pneumonia and sulfapyridine therapy may have played some part in aggravating the prothrombin deficiency. After the patient's fistula had closed spontaneously and she had developed obstructive jaundice, the prothrombin time gradually rose. Another 20 milligram dose of the water soluble ester was given intravenously. The effect of this dose is compared in Chart 8 with the effect of a 10 milligram dose of 2-methyl-1, 4-naphthoquinone given intravenously to patient H. M., with a biliary fistula. Two days after this last dose she underwent an operation which converted the biliary obstruction to a fistula with continuing absence of bile from the intestinal tract for 14 days. Despite this and despite a recurrence of postoperative pneumonia which again was treated by sulfapyridine the effect of this 20 milligram dose of the sulfuric ester was more marked and more prolonged than that of the same dose of the same drug given on an earlier occasion. The caution required in interpreting differences in the effects of drugs given in similar disease states, even in the same patient, is emphasized.

The low blood prothrombin levels of patients with total biliary fistula responded to intravenous vitamin K therapy in much the same way as did those of cases of obstructive jaundice. The characteristic response to vitamin K_1 was shown by M. L. The poorer effects of large doses of the water soluble sulfuric ester of 2-methyl-1, 4-naphthohydroquinone were seen on several occasions in patient M. G. and were compared with the effects of a similar dose of 2-methyl-1, 4-naphthoquinone given to patient H. M. whose prothrombin deficiency seemed to be of the same order of magnitude.

Total biliary fistula may exist for long periods before the development of prothrombin deficiency, Case H. M. This cannot be predicted, however, because both Case M. G. and Case M. L. showed marked prothrombin deficiency within 10 days after establishment of the fistula. In the former case the acute biliary infection before operation and the pneumonia after operation and sulfapyridine therapy may have contributed to the earlier appearance of hypoprothrombinemia. The latter patient, as well, was acutely ill in the immediate postoperative period. Inability to take adequate nourishment by mouth in the early postoperative period was common to all 3 patients.

Hepatitis

The results in hepatitis are shown in the following cases.

C. S. N., No. P.B.B.H. m57021, a 61 year old woman, entered the hospital because of jaundice. At the age of 21 she had had a transient episode of fever and jaundice. For the past year she had felt tired and had taken increasing amounts of alcohol. During the month before entry she subsisted almost entirely on alcohol and had nausea and anorexia accompanied by progressive jaundice. She became constipated, developed abdominal swelling and passed several clay colored stools. For many years she had had occasional epistaxis. In the last month before entry she had noticed a few drops of blood on her pillow every morning.

Examination revealed an elderly, emaciated white woman, obviously ill. Her skin was hot, dry, jaundiced and excoriated, with a few spider telangiectases. Her abdomen was distended, tympanitic, with a fluid level, and slightly tender in both upper quadrants. The liver dulness extended from the fifth interspace anteriorly on both sides of the chest and the liver was smooth and palpable 2 fingers' breadth below the costal margin in the midclavicular line. The laboratory data were as follows: white blood cells 21,000 with 80 per cent neutrophiles; serum protein, 6.5 grams; albumin, 2.1 grams; globulin, 4.4 grams; non-protein nitrogen, 77 milligrams per cent; icterus index, 135. Urine was normal except for the presence of bile. Stools were clay colored. Ascitic fluid was yellow. There were ecchymotic spots about the patient's needle puncture wounds.

She received intravenous glucose and a high caloric diet and seemed to improve for a day or two.

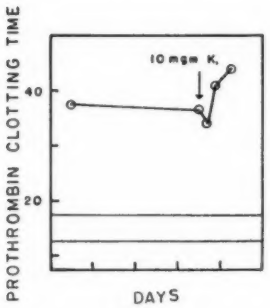


Chart 10

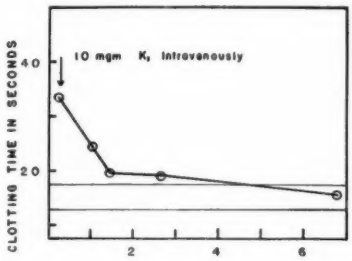


Chart 11

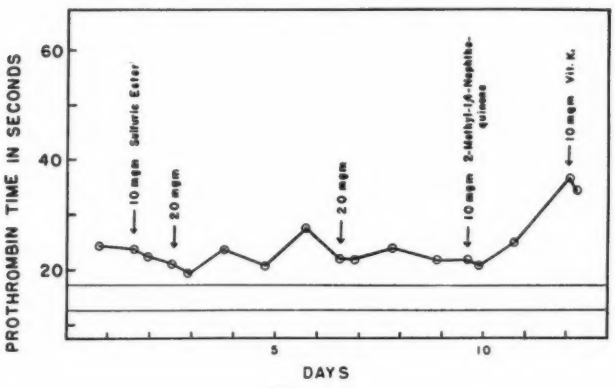


Chart 12

Chart 10. Prothrombin time determinations in case C. S. N., hepatitis.
Chart 11. Prothrombin time determinations in case L. F. D., hepatitis.
Chart 12. Prothrombin time determinations in case S. M., hepatitis.

On the fourth hospital day she became drowsy and jaundice increased. Prothrombin time was 38 seconds. Ten milligrams of vitamin K_1 were given intravenously. The jaundice deepened; the patient lapsed into coma and died on the fifth hospital day.

Autopsy revealed portal cirrhosis of the liver with acute hepatitis and acute suppurative cholangitis. The biliary tracts were not dilated or obstructed. Culture of the liver contained Clostridium welchii and Escherichia coli.

This patient had dietary deficiency, chronic liver disease, and acute liver failure. Chart 10 illustrates the course of the prothrombin levels and shows the lack of response to vitamin K therapy.

L. F. D., No. P.B.B.H. m56922, a 40 year old man, entered the hospital because of epigastric pain and hematemesis of 24 hours' duration. For 20 years he had been a heavy drinker. During the 4 days before entry he drank steadily and ate little food. He had vomited repeatedly during the 24 hours before entry.

Examination revealed an obese white man retching and hiccoughing. The sclerae were icteric and injected. The tongue was dry and coated. The liver extended from the fourth interspace to a level 2 finger-breadths below the costal margin in the midclavicular line. The abdomen was large with tenderness in the right upper quadrant. Laboratory data were as follows: white blood cells, 13,000 with 82 per cent neutrophiles; urine showed albumin and bile, urobilinogen, strongly positive; the stool was brown with bile, guaiac, positive; icterus index, 33; bromsulphalein test showed 30 per cent retention after 30 minutes.

For 2 days the patient subsisted on parenteral fluid only. On the third hospital day he had numer-

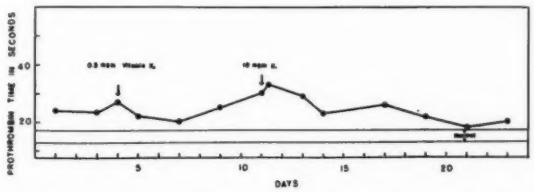


Chart 13. Prothrombin time determinations in case G. B., hepatitis.

ous ecchymoses and some bleeding about the needle puncture wounds. The prothrombin time was 33 seconds. He was given 10 milligrams of vitamin K_1 intravenously. No bleeding was noted thereafter, and the ecchymoses cleared. The patient improved markedly and was discharged well on the fourteenth hospital day.

This chronic alcoholic had an acute hepatitis from which he recovered. The interpretation of the response of prothrombin level to vitamin K therapy must therefore be guarded. The vitamin was given at a time when the patient was acutely ill and was taking nothing by mouth. Chart 11 illustrates the fall in prothrombin time and suggests a definite therapeutic effect. This response was not as rapid as had been noted in cases of obstructive jaundice and biliary fistula.

S. M., No. B.I.H. 50239, a 53 year old man, entered because of progressive dyspnea, ascites, and edema of 6 months' duration. Examination disclosed pallor, slight icterus, massive ascites, and pitting edema from the waist down. The laboratory data were as follows: red blood cells, 3,400,000; hemoglobin, 70 per cent; white blood cells, 4,600; normal differential; most urine specimens contained albumin, bile, and white blood cells; urinary urobilinogen 1:320; stools brown, guaiac, negative; non-protein nitrogen, 39; icterus index, 23; urea nitrogen 9.5; total protein, 4.8; albumin, 1.9; globulin 2.9.

Abdominal paracentesis yielded 2200 cubic centimeters of fluid following which the dyspnea was relieved. Peritoneoscopy disclosed a small, pale, granular liver suggesting portal cirrhosis, and an enlarged spleen. The patient was treated by diuretics, hypertonic glucose intravenously, a high protein diet supplemented by transfusions and liver extract intramuscularly. He lost much of his accumulated fluid but there was no significant improvement in the anemia, the icterus, or the blood protein level. After a month in the hospital the patient suddenly lost consciousness. It was felt that a cerebral vascular accident had occurred. He remained in coma for 48 hours and died.

The prothrombin times in the last 2 weeks of life varied between 20 and 28 seconds, rising terminally. During this period vitamin K was given.

This patient with clinical cirrhosis of the liver had a low-grade prothombin deficiency. The prothrombin time was not altered by repeated large doses of the water soluble sulfuric ester of 2-methyl-1, 4-naphthohydroquinone. To determine whether the lack of response resulted from failure of conversion of the ester to the quinone, perhaps because of inadequate liver function, a large dose of the uncombined naphthoquinone was given intravenously. Again, however, no favorable response was obtained. Vitamin K_1 was given just a few hours before the patient's death so that any effect it might have had could not be determined. The prothrombin levels are recorded in Chart 12.

G. B., No. B.I.H. 55553, a 29 year old white female, entered complaining of swelling of the abdomen and legs of 5 days' duration. She had been jaundiced for a week after scarlet fever at the age of twelve. Mild jaundice had been noted 4 years before admission. Four weeks before admission the present illness started with an acute respiratory infection followed by persistent malaise, weakness, and mild icterus, and then by swelling of the abdomen and eyes. Examination disclosed jaundice, underdevelopment of the breasts, marked ascites, enlarged liver and spleen (palpable after paracentesis), dilated venules over abdomen, edema of lower extremities and sacrum. Laboratory data included: bile in urine; urinary urobilinogen 1:640; white blood cells, 3000; neutrophiles, 84; lymphocytes, 16; icterus index, 20; cholesterol, 152; cholesterol ester, 68; total protein, 5.3; albumin, 1.9; globulin, 3.4; urea nitrogen, 5.8; hippuric acid excretion, 0.58 gram in 4 hours. The bleeding time, 2½ minutes, the clotting time, 3½ minutes, and the prothrombin time, 25 seconds.

Treatment consisted of limitation of fluid intake, high carbohydrate, high protein, low-fat diet, concentrated glucose intravenously, oral and parenteral vitamins A, B group, C, and D concentrates, ammonium chloride orally and mercupurin intravenously, and abdominal paracenteses. During the part of her hospital stay in which she received intravenous vitamin K therapy there was no evidence of improvement either clinically or by laboratory tests.

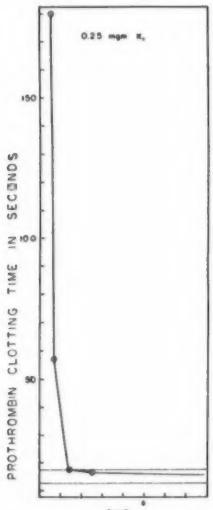


Chart 14

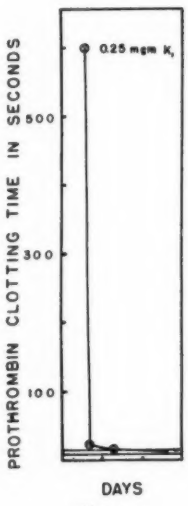


Chart 15

Chart 14. Prothrombin time determinations in case P. A. R., newborn infant.

Chart 15. Prothrombin time determinations in case A. B., newborn infant.

During this period she suffered menorrhagia and intermittent bleeding from the gums.

This patient whose clinical picture suggested chronic hepatitis with acute exacerbation was treated with 0.3 milligram and again with 10 milligrams of vitamin K_1 intravenously. No significant effect was noted. The prothrombin time determinations are shown in Chart 13.

In agreement with Butt and co-workers, and Warner, it was found that the prothrombin deficiency of severe primary liver disease responded poorly to vitamin K therapy. In only one case (L. F. D.) was a significant effect suggested. This was noted in the acute phase of a hepatitis from which the patient recovered.

In the few cases of liver disease studied the prothrombin deficiency was for the most part of low grade, no prothrombin time above 40 seconds being encountered except terminally.

Newborn Infants

The results in newborn infants are presented in the following cases.

P. A. R., No. C.H. 240549[1], a female baby, entered 3 days after a breech delivery. The patient was said to have been cyanotic and limp during the first 3 hours of life. This was followed by muscular twitching and the passage of dark, reddish stools. Physical examination revealed a well developed infant with mild convulsive twitchings of the left extremities, slightly irregular respirations, and rotary nystagmus. The patient was hypotonic and unresponsive. There was a cephalohematoma over the right and left parietal bones. The disc of the left eye was somewhat indistinct, extremities were cold and cyanotic, right arm was limp, and the left arm hypertonic. The prothrombin time on admission was 3 minutes, and the patient was given 0.25 milligram of vitamin K_1 intravenously.

Cerebrospinal fluid was bloody and xanthochromic during the first week, but this gradually cleared. Stools were bloody for a few days but then became guaiac negative. Small ecchymotic spots over the scalp and lower extremities disappeared, and the infant showed marked improvement, but it was felt at the time of discharge that she still had obvious cerebral deficiency.

This newborn baby with hemorrhagic tendency and prothrombin deficiency received vitamin K therapy after intracranial hemorrhage had occurred. The prothrombin time dropped from 180 seconds to normal within 12 hours. The prothrombin times are recorded in Chart 14.

A. B., S.Hosp.[2], a newborn male, was delivered without forceps after labor of 21 hours. Baby was first seen 36 hours after delivery because he was spitting up blood and bleeding from the umbilicus.

Examination disclosed bright blood oozing from the hard palate and fresh bleeding from the umbilicus. Red blood cells, 4,900,000; white blood cells, 16,000; hemoglobin, 104 per cent. Bleeding time was less than 3 minutes, and clotting time less than 5 minutes. The prothrombin time was over 10 minutes.

On the second day of life, the baby was given 0.25 milligram of vitamin K_1. No transfusion was given and the bleeding stopped within an hour. The baby was discharged in good health.

This newborn baby with hemorrhagic tendency and prothrombin deficiency stopped bleeding within 1 hour after vitamin K_1 was given. The prothrombin time dropped from 600 seconds to 21 seconds within 4 hours. The prothrombin time determinations are recorded in Chart 15. In this patient a hemorrhagic

[1]Acknowledgment is made to the Children's Hospital for permission to study this case.

[2]Acknowledgment is made to the Salem Hospital for permission to study this patient.

tendency was associated with a prothrombin deficiency despite normal clotting and bleeding times.

B. H., No. C.H. 244563[1], a 3 day old male baby, entered the hospital because of persistent vomiting since birth. The delivery was at term after a normal pregnancy. Examination of the baby at birth was not unusual; birth weight 7 pounds, 8 ounces. The baby retained nothing taken by mouth from birth. He vomited repeatedly, the vomitus containing bile. Both vomitus and stool were noted to contain blood the day before admission. Saline by clysis and an unknown amount of blood intramuscularly were given 6 hours before admission. On admission, the baby was noted to be dehydrated, the umbilicus and penis were oozing blood, and a needle puncture wound in the heel made 10 hours earlier continued to bleed. The laboratory data included: red blood cells, 5,220,000; hemoglobin, 118 per cent; white blood cells, 11,450; vomitus and stool guaiac, positive; blood culture and serology, negative; capillary clotting time 7 minutes; prothrombin time, 115 seconds.

The baby was given 0.25 milligram of vitamin K_1 intravenously. Within 3 hours the bleeding from the umbilicus, the penis, and the needle puncture wound had stopped, and the capillary clotting time was 3 minutes. The prothrombin time 12 hours after injection of vitamin K_1 was 18.5 seconds. Difficulty in obtaining venous blood prevented further prothrombin readings, but repeated clotting times remained at 3 minutes.

The vomiting continued. Vomitus and stools examined 3 days after the administration of the vitamin were guaiac negative. A diagnosis of duodenal obstruction was made, and laparotomy was done on the eighth day of life, the fifth day after therapy of the hemorrhagic disease. No further vitamin K and no blood were given before operation. At operation, congenital volvulus of the intestine with duodenal obstruction was found and corrected. There was no unusual bleeding during the procedure. The convalescence was uneventful. Transfusions of 65 and 75 cubic centimeters of whole blood were given on each of the first two postoperative days. The baby was able to take food and had gained weight.

Because of the persistent vomiting, the active hemorrhagic tendency could be treated effectively only by the parenteral route in this case. The rapid restoration of normal blood coagulability permitted surgical correction of the duodenal obstruction. A rapid and maintained response to a single dose of intravenously administered vitamin K_1 was noted. It is interesting to speculate on the rôle played by the congenital duodenal obstruction in the development of hemorrhagic disease in this instance.

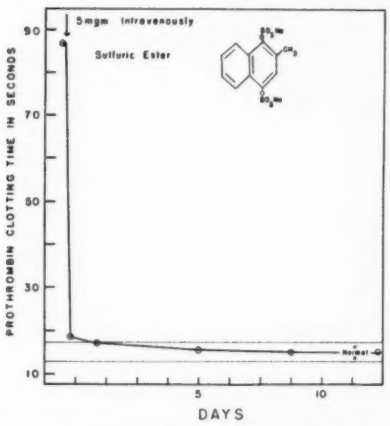


Chart 16. Prothrombin time determinations in case E. S., newborn infant.

D. S., No. B.L.I.H. 29163[2], a male baby, was delivered with low forceps. The patient did not breathe until lobeline was administered. Two days after delivery, bleeding from the forceps scar and bilateral tense cephalohematomas were noted. The baby did not nurse well, had a high-pitched cry, and tense fontanelle. Subdural taps revealed no blood. The prothrombin time was 62 seconds. Five milligrams of the sodium salt of the sulfuric ester of 2-methyl-1, 4-naphthohydroquinone was given intravenously. Bleeding stopped within an hour. The baby recovered.

This newborn baby with hemorrhagic tendency and prothrombin deficiency stopped bleeding within one hour after the water soluble vitamin K preparation was administered intravenously. The prothrombin time dropped from 62 seconds to 24.5 seconds within 3 hours and to 16 seconds within the next 24 hours.

E. S., No. B.L.I.H. 28520[2], a female baby, following a normal, multiparous delivery vomited blood on the second and again in the evening of the third postpartum day. Physical examination was negative. The prothrombin time was 87 seconds. The patient was given 5 milligrams of the sodium salt of the sulfuric ester of 2-methyl-1, 4-naphthohydroquinone intravenously. There was no further abnormal bleeding.

[1]Acknowledgment is made to the Children's Hospital for permission to study this case.

[2]Acknowledgment is made to the Boston Lying-In Hospital for permission to study this case.

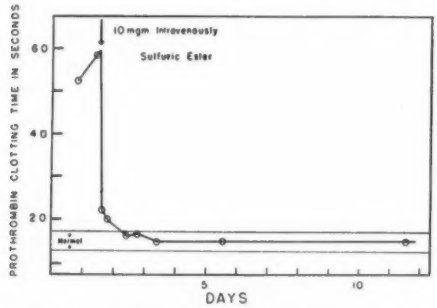


Chart 17. Prothrombin time determinations in case R. MacQ., newborn infant.

This newborn baby with hematemesis and prothrombin deficiency was given 5 milligrams of the water soluble vitamin K preparation. The prothrombin time dropped from 87 seconds to 18 seconds within 4 hours and remained normal thereafter. The prothrombin determinations are shown in Chart 16.

R. MacQ., No. C.H. 238178[1], a male baby, was admitted at the age of one day with history of vomiting blood 14 hours after delivery followed by the passage of grossly bloody stools. At birth the patient had received 30 cubic centimeters of blood intramuscularly. Examination on admission revealed a left cephalohematoma and brisk bleeding from the rectum. Laboratory data included: red blood cells, 2,360,000; hemoglobin, 36 per cent; bleeding time, 15 minutes; capillary clotting time, less than 3 minutes; prothrombin time, 52.5 seconds.

Shortly after admission 75 cubic centimeters of blood were injected intramuscularly. Fifteen hours later the prothrombin time was 58.5 seconds and the baby was given 10 milligrams of the sodium salt of the sulfuric ester of 2-methyl-1, 4-naphthohydroquinone. The abnormal bleeding stopped promptly.

This baby with hemorrhagic disease observed within 14 hours after delivery despite intramuscular blood given at birth, received more adult blood intramuscularly which again failed to lower the prothrombin time or to stop the bleeding. The water soluble vitamin K preparation given intravenously resulted in a drop in prothrombin time to 22 seconds within 4 hours. The prothrombin time determinations are recorded in Chart 17. The gross clotting time in this case was not elevated although the prothrombin clotting time was markedly prolonged and the clinical bleeding was profuse.

Waddell and Guerry; Quick and Grossman (14); Rhoads and Fliegelman; Shettles, Hellman, and Delfs; and Nygaard have reported the successful oral treatment of hemorrhagic disease of the newborn with extracts containing vitamin K_1, or with 2-methyl-1, 4-naphthoquinone. The cases treated with synthetic vitamin K_1 intravenously showed a rapid response to a single small dose (0.25 milligram in 25 cubic centimeters of solution). In no case was a second dose necessary.

The cases[2] treated with the sodium salt of the sulfuric ester of 2-methyl-1, 4-naphthohydroquinone intravenously responded in the same way—5 milligrams of the ester and 5 milligrams of sodium bicarbonate in 5 cubic centimeters of water. Because of the solubility of the sulfuric ester smaller volumes may be used. Alkaline solutions of the sulfuric ester are not light sensitive.

EVALUATION OF STUDY

A group of substances capable of correcting the low blood prothrombin levels of certain clinical and experimental conditions, is described as having "vitamin K" activity. These substances, as found in nature, are all quinones, or are readily transformed into quinones. The quinones are almost completely insoluble in water but dissolve in fat solvents. Vitamin K_1, the original principle as found in alfalfa, has been isolated; its structural formula has been elucidated as 2-methyl-3-phytyl-1, 4-naphthoquinone and it has been synthesized (5, 7). A large group of related compounds has been synthesized and found to have vitamin K activity by chick assay (9). Many of these substances have been used clinically (Fig. 1).

The lack of solubility in water of naturally occurring vitamin K is responsible both for the development of a large part of clinical vitamin K deficiency, and for much of the difficulty of therapy. In obstructive jaundice and in biliary fistula the absence of bile salts

[1]Acknowledgment is made to the Children's Hospital for permission to study this case.

[2]Since these data were compiled a water soluble bisulfite derivative of 2-methyl-1, 4-naphthoquinone (Abbotts hykinone) has been used in hemorrhagic disease of the newborn with similar results—dose: molecular equivalent of 2 milligrams of the naphthoquinone.

in the intestinal tract reduces the absorption of all fat soluble substances. This situation creates the largest group of vitamin K deficiencies. Disease of the gastro-intestinal tract severe enough to interfere with general absorption and nutrition, despite the normal flow of bile, may result in inadequate absorption of vitamin K as shown by altered blood prothrombin levels. It has been pointed out that the liver plays an important rôle in the maintenance of the blood prothrombin. Removal or poisoning of the liver in experimental animals results in a fall in blood prothrombin which cannot be corrected by vitamin K therapy. In clinical liver failure hypoprothrombinemia frequently develops.[1] Investigators have found this condition refractory to vitamin K therapy (4, 23). More recently prothrombin deficiency has been noted in the blood of many newborn infants. The diminution of blood prothrombin is marked in "hemorrhagic disease" of infancy, and readily responds to vitamin K administration.

The earliest efforts at vitamin K therapy made use of crude extracts of varying potency. The isolated principles were used as soon as they became available. Because of their insolubility in water, therapy was largely confined to oral administration, with the addition of bile salts when these were absent from the intestine. The need for an effective parenteral method of therapy became apparent. Nausea, vomiting, intestinal obstruction, or other types of interference with intestinal absorption frequently prevented restoration of normal blood coagulability, often in the patients most in need of effective treatment. Both subcutaneous and intramuscular injection of substances with vitamin K activity proved to have too slow an effect in the presence of bleeding and in preparation for surgery. A method of preparing pure vitamin K_1 in colloidal suspension for intravenous administration has been described (10). This mode of therapy has been found to be rapidly effective, the uncertainties of intestinal absorption are eliminated, and the action of the drug has been noted to be prolonged. 2-Methyl-1, 4-naphthoquinone was effective when used in the same way. On the basis of minimal effective dosages shown by chick assay, 2-methyl-1, 4-naphthoquinone is fully as active as vitamin K_1 (1). However, clinical trials suggest that a single dose of vitamin K_1 has a longer effect than that of an equivalent dose of 2-methyl-1, 4-naphthoquinone.

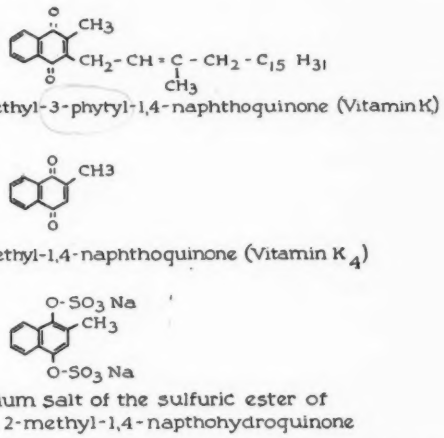


Fig. 1. Formulas for vitamins K_1, K_4, and sodium salt of the sulfuric ester of reduced vitamin K_4.

Several points of physiological interest are brought out by intravenous vitamin K_1 therapy. The blood prothrombin level is very rapidly restored following the correction of vitamin K deficiency. This may occur even in a moribund patient. The prolonged effect of large—10 milligram—doses as compared with that of small—0.5 milligram—doses, suggests the possibility of storage within the body of vitamin K_1, or of some derivative of the quinone. The physical properties of vitamin K_1 suggest that it may not be rapidly excreted. Studies of the complete metabolism of the quinone, however, have not been reported. The intravenous route obviates the changes in chemical form which may occur within the intestinal tract and offers a method for the comparison of the activity of various anti-hemorrhagic substances. Such comparisons must be made with caution in view of the necessarily uncontrolled nature of the clinical experiments.

The search for parenterally effective vitamin K preparations has led to the synthesis of water soluble compounds. The use of these

[1]A review of the evidence for the rôle of the liver in the development of hypoprothrombinemia may be found in a summary by Brinkhous.

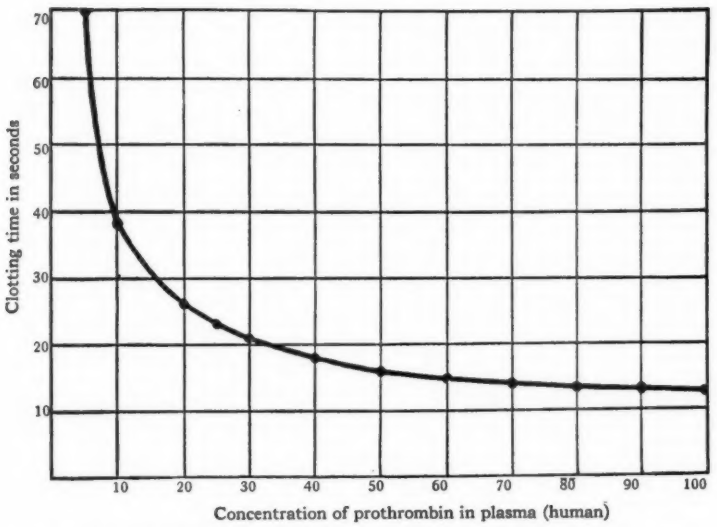


Fig. 2. Determination of prothrombin in human plasma. The relation of the clotting time of recalcified plasma, containing an excess of thromboplastin, to the concentration of prothrombin. (Courtesy A. J. Quick, *J. Am. M. Ass.*, March 14, 1938.)

substances eliminates the need for the large volume of fluid used in suspending the quinone. A report on the intravenous use of a bisulfite derivative of 2-methyl-1, 4-naphthoquinone was recently published by Kark and Souter. They found that 48 hours were required for the return to a normal prothombin time and noted that the effect lasted less than 24 hours. Slow conversion to an active form together with rapid excretion of a water soluble substance may account for these findings. The authors reported no better effect with larger doses. Our experience with a sulfuric ester of 2-methyl-1, 4-naphthohydroquinone disclosed a similar slow and short effect which was not improved by giving 20 milligrams instead of 10 milligrams. The water soluble compounds thus differ markedly from the quinones, in that increasing the dose of the quinones does intensify and prolong their effect.

Reference to Quick's demonstration of the relationship of prothrombin time to concentration of prothrombin (13) demonstrates that the formation of comparatively small amounts of prothrombin will result in a rapid drop from a high to a moderate prothrombin time (Fig. 2), but that larger amounts are required to reduce the prothrombin time to normal. A prothrombin time within normal limits may represent large variations in prothrombin concentration. The prothrombin curves published by Kark and Souter flatten distinctly before the normal level is reached, and a similar effect was noted by us in studying the action of the sulfuric ester and of small doses of the quinones.

Because all other clinical instances of prothrombin deficiency responded to vitamin K administration, the effect of vitamin K on the hypoprothrombinemia of liver disease was studied. The investigation seemed of interest, although we had not encountered a patient with liver disease whose prothrombin deficiency led to abnormal bleeding of clinical significance. Although prothrombin deficiency in liver failure is probably unrelated to vitamin K deficiency, it was thought that an excess of vitamin K might possibly increase prothrombin production. The recognition of small responses to therapy was difficult because the blood prothrombin levels in patients with liver disease were observed to vary spontaneously. In general, the prothrombin deficiency of liver failure was not improved by

vitamin K. In one instance of liver failure from which the patient recovered, a return to a normal prothrombin level followed the administration of vitamin K intravenously. This response was very different from the characteristic reaction to the vitamin in other prothrombin deficiencies in that the return to normal required 72 hours (see Chart 11).

CONCLUSIONS

1. Vitamin K_1—2-methyl-3-phytyl-1, 4-naphthoquinone—can be dispersed in glucose solution and in this form it can be safely administered intravenously.

2. A single 10 milligram dose of vitamin K_1 given intravenously in cases of obstructive jaundice and biliary fistula produced a more rapid and prolonged effect than any other substance so far reported.

3. Single doses of 0.25 milligram of vitamin K_1 or of 5 milligrams of the sodium salt of the sulfuric ester of 2-methyl-1, 4-naphthohydroquinone resulted in rapid cures of hemorrhagic disease of the newborn.

4. The prothrombin deficiency of liver failure did not respond to vitamin K except in one instance in which clinical recovery occurred.

5. 2-Methyl-1, 4-naphthoquinone has been administered intravenously as a colloidal suspension and has been found to be effective by this route.

6. A water soluble sulfuric ester of 2-methyl-1, 4-naphthohydroquinone was capable in 10 to 20 milligram doses of causing distinct drops in prothrombin time, but in the degree, rapidity and duration of its effects, it was found to be inferior to the quinones.

REFERENCES

1. BRINKHOUS, K. M. Medicine, 1940, 19: 329–416.
2. BRINKHOUS, K. M., SMITH, H. P., and WARNER, E. D. Am. J. M. Sc., 1938, 196: 50–57.
3. BUTT, H. R., SNELL, A. M., and OSTERBERG, A. E. J. Am. M. Ass., 1939, 113: 383–389.
4. BUTT, H. R., SNELL, A. M., OSTERBERG, A. E., and BOLLMAN, J. L. Proc. Staff Meet. Mayo Clin., 1940, 15: 69–73.
5. DOISY, E. A., BINKLEY, S. B., THAYER, S. A., and MCKEE, R. W. Science, 1940, 91: 58–62.
6. FIESER, L. F. J. Am. Chem. Soc., 1939, 61: 3467–3475.
7. Idem. Science, 1940, 91: 31–36.
8. FIESER, L. F., and FRY, E. W. J. Am. Chem. Soc., 1940, 62: 228.
9. FIESER, L. F., TISHLER, M., and SAMPSON, W. L. J. Biol. Chem., 1941, 137:659–692.
10. FRANK, H. A., HURWITZ, ALFRED, and SELIGMAN, A. M. New England J. Med., 1939, 221: 975–977.
11. KARK, R., and SOUTER, A. W. Lancet, 1940, 1: 1149–1152.
12. NYGAARD, K. K. Acta obst. et gynec. Scand., 1939, 19: 361–370.
13. QUICK, A. J. J. Am. M. Ass., 1938, 110: 1658–1662.
14. QUICK, A. J., and GROSSMAN, A. M. Am. J. M. Sc., 1940, 199: 1–9.
15. RAVDIN, I. S., and FRAZIER, W. D. Surg., Gynec. & Obst., 1937, 65: 11.
16. RAVDIN, I. S., RHOADS, J. E., FRAZIER, W. D., and ULIN, A. W. Surgery, 1938, 3: 805–814.
17. RHOADS, J. E., and FLIEGELMAN, M. T. J. Am. M. Ass., 1940, 114: 400–401.
18. SHETTLES, L. B., DELFS, E., and HELLMAN, L M. Bull. Johns Hopkins Hosp., 1939, 65: 419–426.
19. SMITH, H. P., ZIFFREN, S. E., OWEN, C. A., and HOFFMAN, G. R. J. Am. M. Ass., 1939, 113: 380–383.
20. STEWART, J. D. Ann. Surg., 1939, 109: 588–595.
21. WADDELL, W. W., JR., GUERRY, J. D., III. J. Pediat., 1939, 15: 802–811.
22. WALTERS, W. Surg., Gynec. & Obst., 1940, 70: 308–318.
23. WARNER, E. D. In discussion on Butt, H. R., Snell, A. M., and Osterberg, A. E. Abstr. in J. Am. M. Ass., 1939, 112: 879–880.

HIP FRACTURES

Treatment by the Multiple Kirschner Wire Method

JOHN B. CHESTER, M.D., F.A.C.S., Fort Lewis, Washington

THE multiplicity of methods used in treating hip fractures is sufficient proof that no perfect method has been evolved. The percentage of results which might be classified as excellent, or even satisfactory, is still too low, though unquestionably far greater than was the case 10, or even 5, years ago. The reasons for being unable to evolve a universally successful method of treatment are perhaps insurmountable. Probably chief among these is the fact that this fracture is common in the aged and relatively rare in youth. A mechanical reason is the difficulty of proper reduction due to the freely movable billiard ball like femoral head unattached or held by any strong ligament, with the added possibility of interposition of torn capsule. A still further reason, physiological in nature, and probably more important in the case of the femoral neck as opposed to intertrochanteric fractures, is the fact that the main blood supply of the femoral head is derived from capsular arteries which enter the base of the neck extending into and anastomosing in the head. When this blood supply is broken off, unless restored by good and close approximation of the fragments, death and aseptic necrosis of the head will surely result. It has been conceded by almost all orthopedists that the minute blood supply through the ligamentum teres is not sufficient to nourish the head; so in order to prevent death of the fractured head and nonunion, it is absolutely essential to procure early reduction and firm fixation of the fragments so that the disrupted circulatory lines of communication will be quickly re-established. This aseptic necrosis of the head has been recognized for a great many years, being first described by Sir Astley Cooper over a hundred years ago, and as late as 1896 Kocher thought that death and aseptic necrosis of the head took place in *all* femoral neck fractures.

A brief review of the evolution of the treatment of hip fractures recalls that the first great advance was introduced by Whitman in 1912 and consisted of his classical reduction by abduction, flexion, extension, and internal rotation followed by fixation in a body plaster spica. With the Whitman technique, bony union was not claimed for more than 40 to 60 per cent of cases. Its most serious defect was the prolonged immobilization leading to pulmonary complications in the aged. This fact was a stimulus to orthopedists in the development of methods which would not only give firm fixation but also allow early mobilization of the patient. To fill both of these requirements some form of mechanical fixation was obviously necessary. However, until the work of Smith-Petersen, first published in 1931, mechanical fixation had been largely limited to the use of the round nail or bone peg driven through the trochanter into the head. In the case of the former, fixation was not complete due to rotation of the head on the nail which served as an axis. In the case of the latter, fixation was very unstable due to weakness and frequent breakage of the bone peg. Smith-Petersen overcame this disadvantage of the nail by developing a flanged nail which definitely prevented rotation of the fragments. His nail was later greatly improved by canalization (Johansson), which allowed more accurate insertion of the nail over a Kirschner wire. Since his pioneer work, a number of mechanical devices have been developed which have certain advantages over the nail in that they not only fix but impact and hold the fragments in impaction. Examples are the Henderson lag screw, the Morrison lock bolt, the Moreira stud bolt screw, the Martin multiple screws, and many others. All of these methods of mechanical fixation require a rather elaborate armanentarium to be carried out properly, not to speak of considerable practical experience not available to all surgeons required to treat hip fractures. In the absence of these two requirements, depressing accidents occur, the most common of which is splitting of the trochanter major, neck, or the femoral head itself (Fig. 1). Suffice it to say, hip fractures are one condition in which accidents are an ill afforded luxury, permanent crippling of the patient being the usual unfortunate result. When this happens, just as usual, little can be done to improve the patient's condition.

It is the purpose of this paper to present our experience with as near a foolproof mechanical method of fixation in hip fractures as we believe has yet been devised. The multiple Kirschner

Medical Corps, United States Army.

wire method apparently was first used extensively in this country by Dyas and Aries, of Chicago, who published their results in the October, 1936, issue of SURGERY, GYNECOLOGY AND OBSTETRICS. This method had been previously used, though not so successfully, by orthopedic surgeons in Norway and other countries. Since publication of the Dyas and Aries article, there have been several other articles published by men who tried the method with less success; in fact, most of the publications since were for the purpose of condemning the method. However, it would appear that most of the reasons given for this condemnation were the result of carelessness in the hands of the orthopedists who had used it rather than of any inherent fault in the method itself. One criticism is that there is danger of drilling the Kirschner wire through the acetabulum into the pelvis and puncturing some of the large vessels. In careless hands this has actually happened but is inexcusable. Others have stated that the wires tended to migrate, either burying themselves in the bone so as to make removal difficult (Fig. 6 c) or even going so far as to lose themselves in the soft tissue or pelvis. The first argument might as reasonably be used against surgical opening of the abdomen or any other surgical procedure in which accidents caused by the operator's carelessness might occur. The second accident noted can easiy be prevented as will be shown.

Advocates of the flanged nail have claimed more speed for their method. Even if true, we do not consider speed to be a great necessity when the technique is practically shockless. However, when the nail is threaded over a Kirschner wire, we have found it usually necessary to insert several wires before the accurate placement or centering necessary for use of the nail is secured. When this

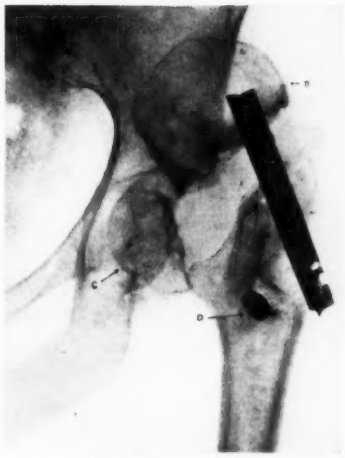


Fig. 1. Female, aged 70 years. Accident resulting from the insertion of a Smith-Petersen nail. Roentgenogram made 3 years after original nailing. Patient was brought to my attention by medical service to which she was admitted for generalized arteriosclerosis and cardiac disease. She had been bed-ridden since operation. *A*, Sclerotic blood vessel; *B*, apparently portion of greater trochanter; *C*, partially absorbed femoral head; *D*, cap of Smith-Petersen nail.

a b c

Fig. 2. Female, aged 56 years. a, Impacted femoral neck fracture. Fracture 1 month old and patient in body spica cast when first seen. Fragments in satisfactory position. b, Same case, 90 days after injury. c, Five months after injury and 2 weeks after removal from cast showing loss of impaction and loss of reduction. This accident could almost certainly have been avoided and patient spared the discomfort of a body cast by the insertion of several Kirschner wires to be kept in place for 8 to 12 months.

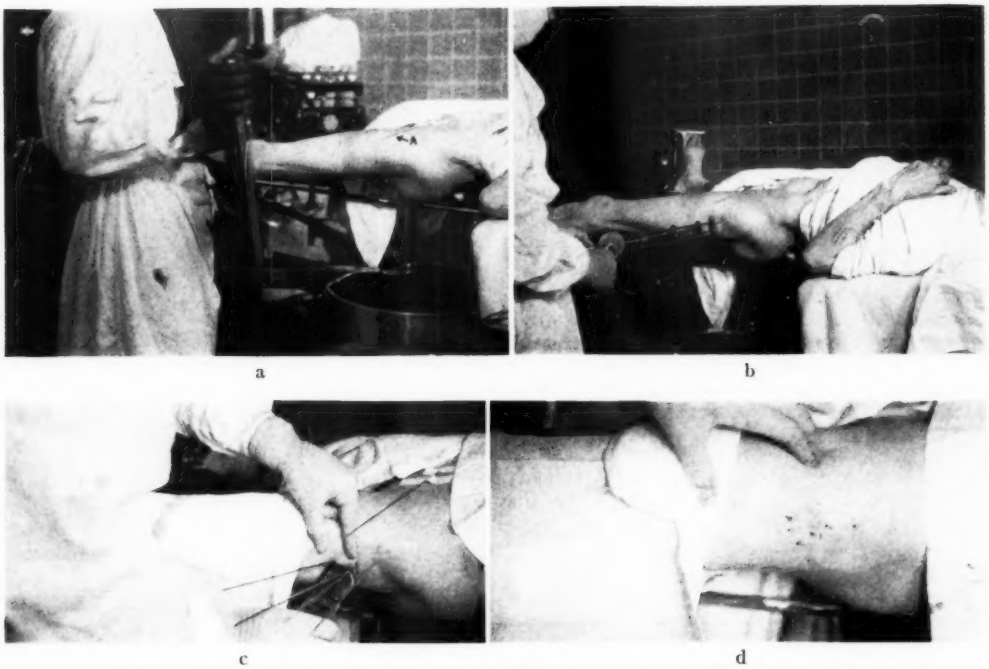


Fig. 3. Case 1. Male, aged 54 years. a, Fracture has been reduced by manipulation under local anesthesia and is held fixed by Scanlon-Balfour table. Photograph shows preparation for check of position by lateral roentgenogram. Curved casette with portable machine placed laterally is better if available. Note guide wire *A* extending from greater trochanter and bisecting Poupart's ligament. b, Insertion of first Kirschner wire. Note circle of skin anesthesia about area through which wires will be passed. Known position of guide wire with relation to femoral neck assists in determining direction of Kirschner wire. c, Kirschner wires being clipped after checking proper depth and position by x-ray film. Wires should be bent at bone surface before clipping to prevent occasional complication of migration (Fig. 4e). Skin about wire depressed before cutting of wire ends. d, Operative site immediately after wires have been clipped below skin level and skin allowed to cover all wire ends. Operation has been completed and no further fixation of fracture is required in most instances.

is necessary the Kirschner wire method might require less time than the nailing operation.

We first began using this method of treatment in hip fractures in December, 1936, after publication of the work of Dyas and Aries. With minor changes in technique it has since become routine with us whenever applicable. When properly applied the technique is one which is almost entirely free of shock to the patient, requires no skin incision, and yet fulfills the two criteria of firm fixation of the fracture with early mobilization of the patient. It consists essentially of the fixation of the fragments by the insertion of multiple Kirschner wires so placed as to utilize the crossed nail locking principle well known to carpenters. In other words, the wires are placed at widely varied angles which locks the head in place in a manner impossible for wires placed in parallel planes. We first attempt to secure accurate reduction of the fracture. This is done manually after the patient is placed on the fracture table and the well leg is fixed in the foot piece so as to anchor the pelvis firmly. We have found local anesthesia perfectly satisfactory for accomplishing reduction.

Preoperative preparation is important. Our custom is to administer one of the barbiturates the night before the operation and again 30 minutes before taking the patient to the fracture room. Morphine from 1/6 to 1/4 grain and scopolamine 1/200 grain are given at the same time. With this preparation we have found the patient to sleep intermittently throughout the operation, and shock incident to the trauma involved is minimal or absent. In the administration of the local anesthetic we attempt to locate the joint

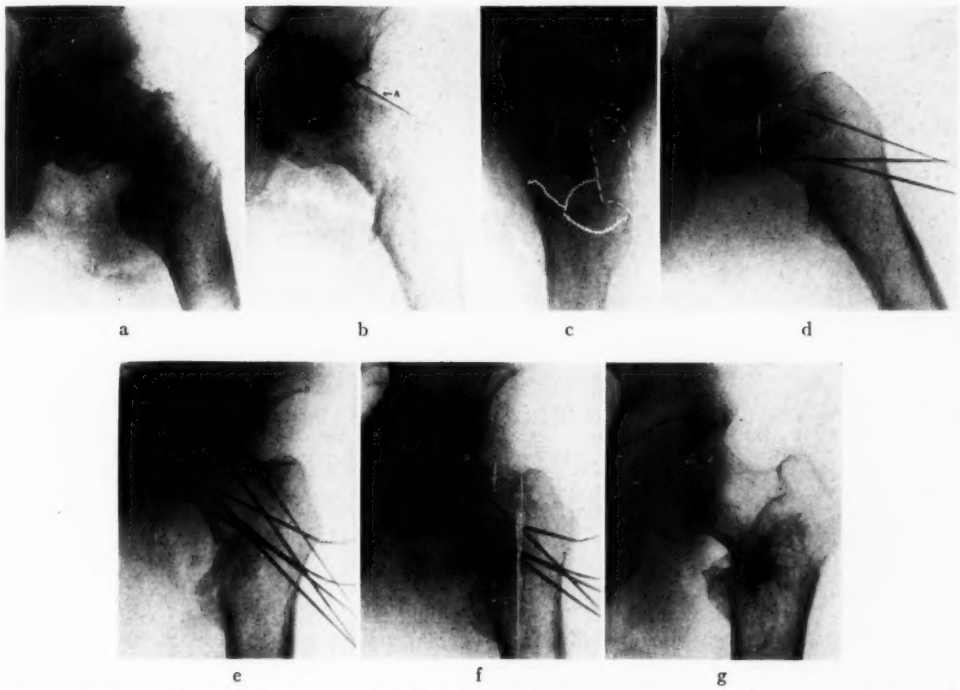
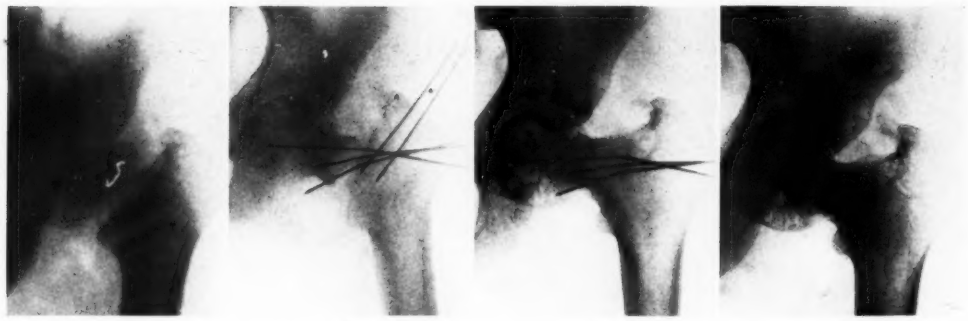


Fig. 4. Case 1. a, X-ray film, anteroposterior view, of fracture through base of femoral neck and trochanters before reduction. b, Same patient after reduction showing external guide wire *A* following fairly accurately the normal line of the femoral neck. This x-ray film corresponds to photograph, Figure 3a. c, Lateral view proving accurate reduction. d, After insertion of 2 Kirschner wires purposely not far enough. e, After insertion of all 5 wires. Two wires have been bent near bone surface. Remaining 3 will be similarly bent before clipping. The small sixth wire is the externally placed guide wire. f, Immediately following bending and clipping of wires. g, After 14 months and immediately after removal of wires. Weight bearing for past 9 months. Firm bony union is present and the removal of the wires could have been done with safety several months earlier.

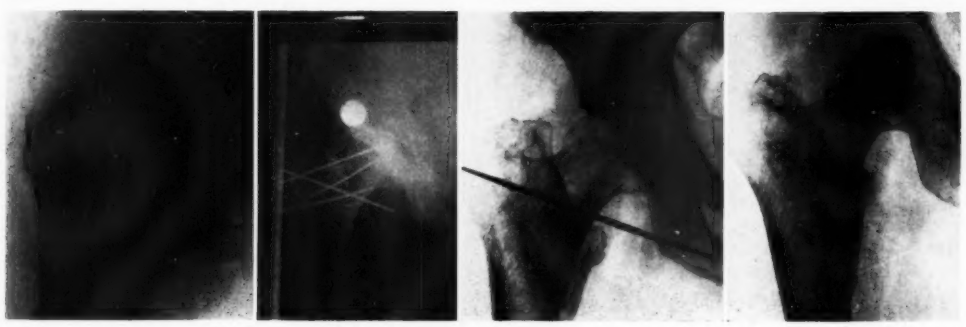
capsule by introduction of a long needle until bloody synovial fluid can be aspirated and then we inject 20 cubic centimeters of 2 per cent procaine directly into the joint. If difficulty is met in definitely locating the joint capsule, the anesthetic may be merely injected about the joint, slightly more being required in this event. Reduction is accomplished manually by a manipulative method which combines portions of the technique of both Ledvetter and Whitman, varied, of course, with the different types of fractures. Essentially, it consists of flexion of the joint to about 35 degrees, external rotation, abduction, traction, followed by internal rotation and extension accomplished in one movement. We sometimes find it necessary to vary this by having an assistant apply lateral traction to the hip by pulling laterally on the upper thigh while manipulation is being carried out. After completion of the manipulation, the involved extremity is fixed in abduction, extension, and internal rotation by fastening the foot to the footpiece of the fracture table. Before reduction is checked by roentgenography, a Kirschner wire is fixed to the skin anteriorly bisecting Poupart's ligament and pointing outward and downward to the small angle formed by the junction of the greater trochanter with the shaft (Fig. 3a). This guide wire so placed usually follows fairly accurately the normal line of the femoral neck. Roentgenograms, both anteroposterior and lateral, are now made with the portable machine to check reduction. If satisfactory, we are ready to proceed with the insertion of the Kirschner wire drills. The guide wire previously noted is now indispensable in indicating the direction for inserting the wires in the horizontal plane. For the vertical plane, fixation of the extremity at 25 degrees



a b c d

Fig. 5. Case 2. Male, aged 19 years. a, Roentgenogram of fracture of base of femoral neck showing marked rotation and displacement. b, This patient, a C. C. C. enrollee, was admitted 2 months after injury and, because of fixation, accurate manual reduction was not possible. Open reduction using the Ollier approach was done. Fragments freshened, approximated, and fixed by 3 Kirschner wires. Trochanter major *A*, which was removed with muscle attachments for exposure, reattached with 2 crossed Kirschner wires *B*. Traction was applied to this patient for 6 weeks. On removal angulation at fracture site promptly took place with bending of wires. Use of 2 more wires originally would undoubtedly have prevented this. c, X-ray film taken 8 months after operation showing firm bony union. Wires holding trochanter removed after 10 weeks. Wires through neck allowed to remain for 12 months. d, Immediately after removal of wires. Three-quarters of an inch shortening due to varus position of neck caused by original angulation and bending of wires at site of fracture. Function normal.

internal rotation results in an almost flat plane of the neck parallel to the floor. For anesthesia at this point, we find that it is sufficient to anesthetize a fairly wide circle of skin extending from approximately ½ inch below the trochanter major to its upper border. This leaves the area directly over the point of insertion of the wires uninfiltrated, so that one is allowed to palpate the bone with relative ease. Two 16-gauge Kirschner wires are now passed through the lower portion of the trochanter, or shaft just below the trochanter, into the neck and head of the femur, the guide wire being used to determine direction (Fig. 3b). These 2 wires are purposely *not* inserted far enough so as to avoid any danger of inserting them too far (Fig. 4d). Another anteroposterior and lateral check at this point enables us to determine by measurement on the roentgenogram, the exact distance necessary further to insert the 2 wires. Accuracy is obtained by nicking the wires at this exact distance from the skin and then continuing their insertion until this nick reaches the skin. We now have 2 wires properly placed and their direction accurately checked on the roentgenogram. By the use of these as guides and direction finders, the remaining 3 wires can be easily inserted to the proper depth and in the proper direction. After all 5 wires are in place, it is



a b c d

Fig. 6. Case 3. Female, aged 74 years. a, Comminuted, intertrochanteric fracture, right hip. b, After fair reduction and fixation by 4 Kirschner wires. This was an early case and wires were not bent at bone surface, resulting in migration of upper wire as shown in Figure 6c. c, After removal of 3 wires. The fourth wire has migrated to trochanteric surface and required an incision for removal. d, X-ray film after 1 year showing solid bony union.

a b c d

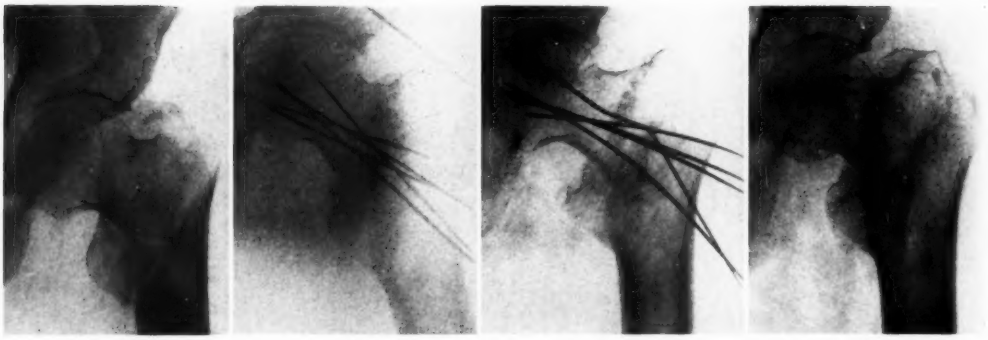
Fig. 7. Case 4. Male, aged 39 years. a, Comminuted fracture through base of femoral neck, right hip. b, After reduction and fixation by 5 Kirschner wires crossed at widely divergent angles. Upper wire A inserted a fraction too far, but caused no symptoms even after beginning weight bearing. c, Lateral view immediately after reduction and wiring. A poor film but shows all wires to be within the femoral neck. d, X-ray film made 8 months after injury and immediately after removal of wires. Weight bearing for past 4 months. Firm bony union.

our practice to take a third series of roentgenograms to check the position of the wires. If all is satisfactory and no further adjustments are necessary, each wire is grasped in turn and sharply angled at its point of exit from the femur, after which, the skin is pressed down approximately 3/8 inch at which point the wires are cut and the skin allowed to come out over the ends of the wires leaving a closed operative field (Fig. 3, c and d). Bending the wires at the bone is important, as it will definitely inhibit the migration or slipping of the wires further into the bone, a point of objection to this method raised by some orthopedists as we have already noted.

The operation is now complete, and it is optional with the surgeon whether or not he wishes to apply skin traction at the extremity for a few days until muscle spasm, normally present in any fracture, has been overcome. In our own clinic, we vary this with the urgency of getting the

a b c d

Fig. 8. Case 5. Female, aged 49 years. a, Fracture of femoral neck at attachment of head. b, Anteroposterior view immediately after reduction and fixation by 2 stainless steel drills and 2 Kirschner wires. Heavy drills used in this case because of fear that small caliber wire would not hold firmly in spongy capital bone since fracture is so proximal as to involve upper portion of head. c, Lateral view showing that one wire had missed the fracture line entirely. The other wire had made exit from neck but re-entered head. Two pins are well within femoral neck throughout. This picture illustrates the importance of final lateral views in all cases so that useless wires may be withdrawn and replaced. d, X-ray film made after 6 months showing evidence of bony union. Pins and wires removed earlier than usual because of irritation caused by the pins. Local infection and periostitis followed removal of pins. This is the only case in a series of 23 in which heavy pins were used and the only case in which infection occurred.

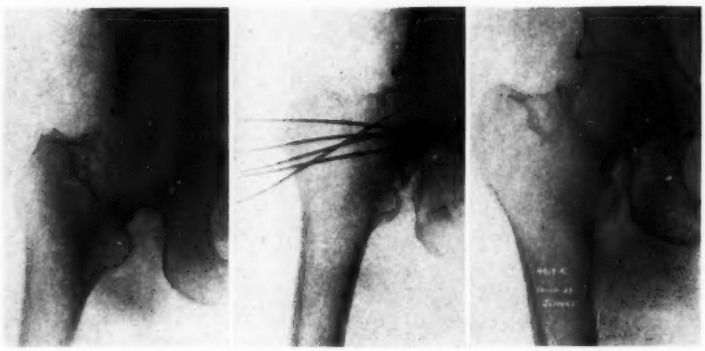


a b c d

Fig. 9. Case 6. Male, aged 62 years. a, Comminuted intertrochanteric fracture, left hip. b, Anteroposterior view after reduction and transfixion by 5 Kirschner wires. Upper wire inserted too far and slightly retracted before clipping. Lateral view in this case showed 4 wires completely within the femoral neck, the fifth leaving the neck but re-entering the head causing result shown in Figure 9d. c, X-ray film taken after 6 months showing firm bony union. One wire, apparently the one which made exit from the femoral neck, being bent. d, Roentgenogram taken 8 months after injury and 1 month after the removal of the wires.

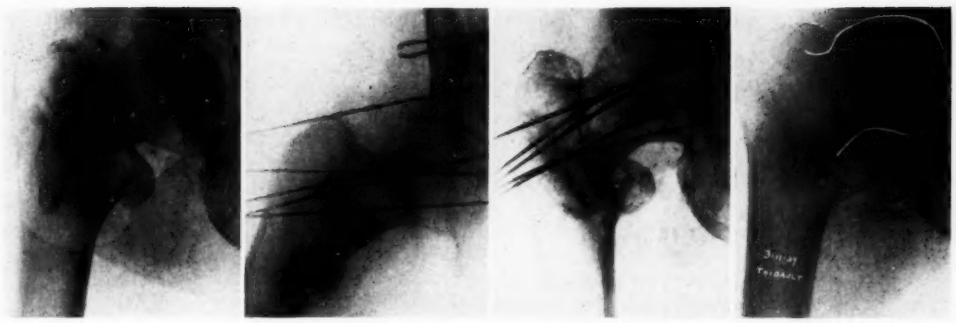
patient up immediately. If the patient is old and in poor general condition, no traction is applied. If young, strong, and heavily muscled, the maintenance of about 10 pounds of traction for 10 days to 2 weeks will probably be more comfortable for the patient.

As for the number of wires used, we have arbitrarily used 5 in this clinic because we have found that 3 wires will bend (Fig. 5b), while 5 wires never have in our experience. We ordinarily use stainless steel Kirschner wires leaving them in place from 8 to 10 months or even longer, dependent on evidence of union as shown by the roentgenogram. The longest period in this series has been 14 months (Case 1). In no case have we observed x-ray findings of irritation in the host caused by the wires. As previously stated, we have found it safe to allow the patient up immediately in wheel chair, and after 6 to 8 weeks, on crutches. We have not allowed weight bearing until some evidence of union is present. When weight bearing is started, no inconvenience is caused by the presence of the wires under the skin except that in some cases the patients complain of a pricking sensation where the end of the wire was perhaps left unusually long or has become too long by extrusion, an event which occasionally takes place.



a b c

Fig. 10. Case 7. Female, aged 56 years. a, Impacted fracture mid-portion of femoral neck. b, Same case immediately after transfixion by 5 crossed Kirschner wires. This case, requiring no reduction, was done on fluoroscopic table. c, After 10 months and immediately after removal of Kirschner wires. X-ray evidence of firm bony union. Weight bearing, and symptom free for past 6 months.



a b c d

Fig. 11. Case 8. Male, aged 68 years. a, Anteroposterior view showing comminuted fracture through base of femoral neck and through trochanters. b, Immediately after reduction and after insertion of 4 wires. Two lower wires inserted too far and required slight withdrawal. Upper wire is the external guide wire. c, X-ray film taken 4 months after injury showing 5 wires in position. The cause of the bend in 1 wire is undetermined. d, Anteroposterior view 8 months after injury, and 2 weeks after removal of wires. Note that bony union is complete. Full weight has been borne since 3 months before removal of the wires.

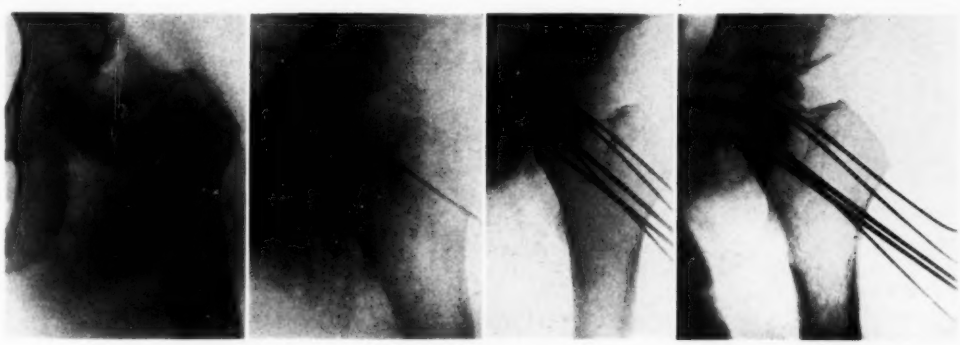
A few rules or words of caution might be of value:

1. Reduction should be as nearly perfect as possible. Odds in favor of nonunion or absorption of head are in inverse ratio to accuracy of reduction.

2. Lateral x-ray checks are essential for reduction, of course, but also to check the wires. A wire which does not traverse the fracture line and stay within the femoral neck and head throughout its course in both the anteroposterior and lateral views is useless and should be removed and reinserted. An exception to this rule is shown in Figure 8c; here a wire leaves the neck and reenters the head.

3. To identify the wires on the film, it is helpful to clamp forceps of different shapes or preferably small lead markers to the Kirschner wires before roentgenograms are made.

In impacted hip fractures in good position there is a tendency on the part of many surgeons to leave well enough alone. In these cases we believe that wiring should always be done. If no reduction is necessary, the wires may be inserted quickly on the fluoroscopic table under direct vision with practically no shock and little inconvenience to the patient (Fig. 10). One does not then have to fear that the impaction will become loosened and the reduction be lost as happened to



a b c d

Fig. 12. Case 9. Female, aged 54 years. a, Comminuted fracture through distal portion of femoral neck. b, Immediately after reduction showing relation of external guide wire to normal line of femoral neck. Slight varus obtained in this case improves chances of bony union. c, After insertion of 5 Kirschner wires. d, After 5 months. X-ray evidence of definite bony union is shown. There is no evidence of angulation, or bending of the wires, despite the fact that this patient weighed more than 200 pounds and was unrestricted as to movement. Full weight bearing is still prohibited at this time because of this excessive weight.

one of our patients several years ago (Fig. 2). Since this unfortunate experience, we have wired impacted hip fractures as a matter of routine.

As for use of the fluoroscopic table routinely in impacted cases, we do not recommend it unless one is fortunate enough to have a modern combined fracture fluoroscopic table. We believe that the ease of reduction and fixation of the patient on a good fracture table outweighs the advantages of fluoroscopy despite time wasted while waiting for development of repeated series of films. A portable fluoroscopic headpiece is perfectly useless in hip fractures. An additional disadvantage of the fluoroscopic technique is exposure of the operator which this method entails. Satisfactory methods of shielding the orthopedist's hands from the rays have yet to be devised, and so much unavoidable fluoroscopic work is necessary in a busy orthopedic clinic that whenever possible it should be avoided.

Roentgenographic case records are presented to illustrate special features of the technique. In their selection an effort has been made to include as many different types of hip fractures as possible (Figs. 4 to 12).

CONCLUSIONS

Further data with reference to the multiple Kirschner wire method of treatment in hip fractures are presented. Cases illustrating various types of hip fractures are demonstrated.

The writer has used this method in 23 patients over a period of 3½ years. Five are under treatment and cannot be classed as cures, but all show x-ray evidence of union. Eighteen patients are cured. There has been 1 case of infection in which 2 nails and 2 wires were used (Case 6). The ultimate outcome of this case must be classed as doubtful. No case of nonunion has occurred.

The relative simplicity of this method and uniformly good results possible under proper application together with minimal surgical shock warrant a more thorough test and widespread use.

Photography by U. S. Army Signal Corps, Fort Sam Houston, Texas.

REFERENCES

1. Backer-Grondahl, N. Surg., Gynec. & Obst., 1937, 64: 1073.
2. Bosworth, D. M. West. J. Surg., 1936, 44: 4847.
3. Breck, Louis W. Southwest. Med., 1939, March, pp. 72–78.
4. Colton, F. J. Am. J. Surg., 1937, 38: 619–628.
5. Creyssel, J., and Roulet, L. Schweiz. med. Wchnschr., 1939, 69: 637–640.
6. Dyas, Frederick G., and Aries, Leon J. Surg., Gynec. & Obst., 1936, 63: 499–503.
7. Grinda, J. P. Monde méd., 1936, 46: 735–738.
8. Krapp, H. Zentralbl. f. Chir., 1935, 62: 2706–2709.
9. Moene, I. Norsk. Mag. f. Laegevidensk., 1935, 96: 1268–1297.
10. Moore, A. I. Internat. Surg. Digest, 1935, 19:323–330.
11. Selig, S. J. Bone & Joint Surg., 1939, 21: 182–186.
12. Smith-Petersen, M. N. Surg. Gynec. & Obst., 1937, 64: 287–295.
13. Thorton, L., and Sandison, C. South. M. J., 1936, 29: 456–460.

A ONE STAGE OPERATION FOR THE CURE OF CARCINOMA OF THE AMPULLA OF VATER AND OF THE HEAD OF THE PANCREAS

I. RIDGEWAY TRIMBLE, M.D., JOHN W. PARSONS, M.D., and CLAUDE P. SHERMAN, M.D., Baltimore, Maryland

THE operative story of growths in the region of the head of the pancreas and in the second portion of the duodenum is of great interest to all physicians and surgeons both because of its constant challenge and because at the present time the only effective operation shuts off permanently the external secretion of the pancreas without apparent significant effect upon the health of the patient. This story, although commenced in 1888, has not been one of rapid progression toward successful removal characteristic of many other abdominal operations for malignant growths since that date. Factors obviously responsible for this delay are, as stated by Judd and Hoerner, (1) the insidious onset of the disease, (2) the generally poor condition of the patients, (3) the relative inaccessibility of the lesions, (4) the proximity of important structures which cannot be sacrificed, and (5) the extreme technical difficulties of the procedure. Although the operation here described was performed to remove a carcinomatous growth arising from Vater's ampulla, the same operative technique may be applied to other tumors in this whole periampullar area whether they arise from the duodenal wall, the common duct, the pancreatic duct, or the head of the pancreas.

That carcinoma of the ampulla of Vater is insidious in its onset is well known, and a positive diagnosis is a matter of great difficulty and has comparatively seldom been made before operation. There is no pathognomonic nor even any constantly recurring symptom, although jaundice is by far commonest. This is usually gradual in onset and progressive, although there may be a distinct intermittency (due probably, as Outerbridge suggests, to turgescence and vascularization of the neoplasm) as opposed to carcinoma of the pancreas in which the jaundice is more apt to be steadily progressive.

Associated conditions such as pruritus will, of course, accompany or follow the jaundice. This was the first and for several months the most distressing symptom in the case here reported. Afterward come anorexia, rapid loss of weight, and more or less pronounced decoloration of the stools, amounting in some instances to complete acholia. Next in frequency, in approximately one-half the cases, comes pain, either in the epigastrium, gall bladder, liver region, or back.

The conditions with which cancer of Vater's ampulla is most likely to be confused are obstruction of the common duct by stone, benign stenosis from scar formation, chronic interstitial pancreatitis, and cancer of the head of the pancreas. Expectant treatment of some of these conditions may be wise; but to temporize too long or to split hairs in attempting to establish a diagnosis in the presence of a malignant growth at the ampulla of Vater may render removal impossible because of extension or metastases, or may make the patient, because of the harmful consequences attendant on biliary obstruction, a poor or prohibitive operative risk. Metastases are rarely found in a patient with cancer of Vater's ampulla; this fact is of course favorable and is a stimulus toward attempted operative cure. On the other hand, this freedom from metastases is also indicative of an unfavorable fact—that a patient with such an obstruction of the biliary and pancreatic ducts succumbs rapidly, too soon for metastases to occur. The average duration of life in 47 cases studied by Outerbridge was only 7½ months; in 23 cases it was less than 6 months; and in 10 cases less than 3 months. Upcott writes: "There is probably

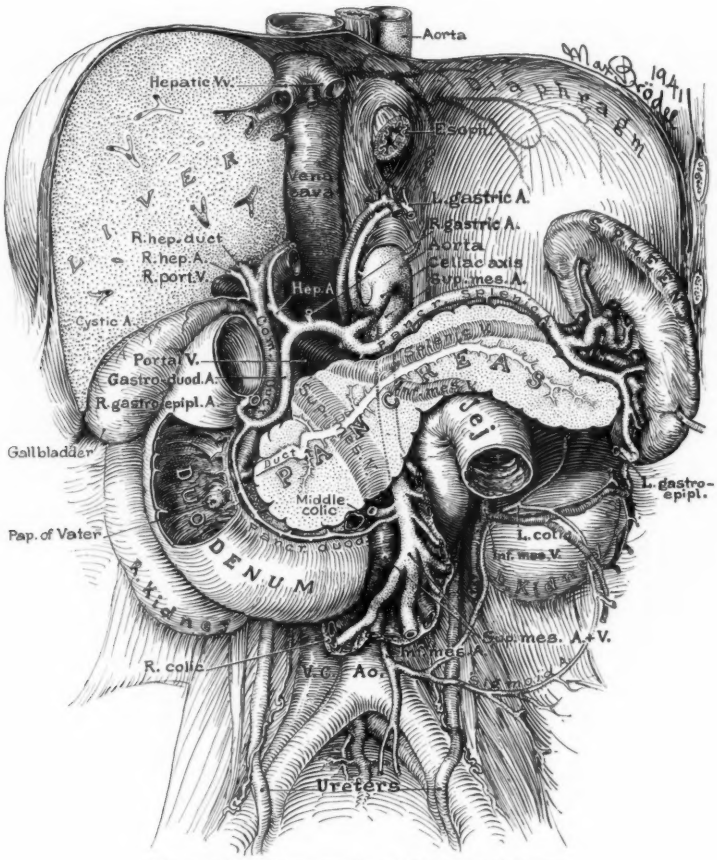


Fig. 1. Normal topography of the upper abdomen.

no position in the body outside the central nervous system where a growth, while yet so small, is heralded by more widespread symptoms." Boyce states: "These symptoms are due to obstruction of the bile flow or of the pancreatic flow or of both, and they lead with incredible swiftness to hepatic insufficiency, pancreatic insufficiency, and the hemorrhagic diathesis which is one of the most frequent and most dangerous complications of obstructive jaundice of any origin. In other words, they are manifestations of pathologic states which are compatible with life for only a limited period of time."

The anatomical situation of a growth involving the second portion of the duodenum, the bile and pancreatic ducts, and the head of the pancreas makes a surgical attack a formidable procedure because of the relative inaccessibility of the lesion. The pancreas is situated transversely across the posterior wall of the abdomen, at the back of the epigastric and left hypochrondriac regions, with its head embraced in the concavity of the curve formed by the first, second, and third portions of the duodenum. The posterior surface of the pancreas is not covered by peritoneum and is in direct contact with the vena cava, which lies between the pancreas and the vertebral column; the portal vein, which lies behind the head of the pancreas; its tributary veins, the inferior mesenteric, superior mesen-

teric, and splenic veins; the abdominal aorta; the splenic artery; and the origin of the superior mesenteric artery.

Anteriorly the pancreas is covered with the peritoneum of the omental bursa, which separates it from the overlying stomach, transverse colon, and transverse mesocolon. Just at its superior surface is the celiac axis and its branches; its inferior surface is in contact with the transverse portion of the duodenum and the duodenojejunal flexure (Fig. 1).

The secretion of the pancreas in man is quite abundant, being 500 to 800 cubic centimeters a day, and its digestive action depends upon its three groups of enzymes—proteolytic, amylolytic, and lipolytic. Evidently the proteolytic enzyme of the juice is secreted in a zymogen or pro-enzyme form (trypsinogen), which is activated or converted to trypsin by something contained in the mucous membrane of the small intestine (duodenum, jejunum). Pavlov supposed this substance to be an enzyme, and called it kinase or enterokinase, which by hydrolytic action upon the trypsinogen converts it into trypsin. Trypsin acts with another important proteolytic enzyme of the pancreas, erepsin, to split the protein molecule into its constituent aminoacids.

The starches are acted upon by the diastatic enzyme (amylase), which is found in the secretion of the pancreas or in an extract from the gland. Its action is similar to, or identical with, that of ptyalin, causing a hydrolysis of the starch, with the production of maltose and acro-odextrin. Before absorption these substances are further acted upon by the maltose of the intestinal secretion and converted to dextrose.

The third important class of enzymes in the pancreatic juice attacks neutral fats through an active enzyme, lipase, capable of hydrolyzing or saponifying these fats, breaking them up into glycerin and the constituent fatty acid. It should be added that the action of this enzyme is aided very materially by the presence of bile. Although this latter secretion contains no lipase itself, nevertheless mixtures of bile and pancreatic juice split the neutral fats more rapidly than does pancreatic juice alone.

Faced with a growth at the ampulla of Vater obstructing the common duct, the surgeon has the choice of three operative procedures: (1) leaving the growth in place and short-circuiting the flow of bile by an anastomosis between the common duct or gall bladder and the stomach or intestine; (2) incision of the duodenum, local removal of the growth, and fixation of the stumps of the common and pancreatic ducts to the duodenum at the same area from which the tumor was excised; (3) radical removal of the growth by resection of the first and second portions of the duodenum. Continuity of the gastrointestinal tract must then be re-established by an anastomosis between the stomach and the jejunum, and of the biliary tract by an anastomosis between the stump of the common duct or the gall bladder and the stomach or intestine. Neither of these procedures restores the channel of the pancreatic duct for the flow of bile into the intestine, and the re-establishment of this flow has been the most baffling problem to the surgeon, the real *bête noire* which has been the cause of operative timidity and of consequent delay in the surgical answer to this whole question. Attempts at such a reconstruction, after a sufficiently wide resection of the tumor, have resulted in a high incidence of leakage of both pancreatic and duodenal secretions, with the resulting prohibitive mortality.

Operations for diseases of the pancreas itself preceded by 10 years those for a tumor at the ampulla of Vater, but those paved the way for these because the field and the operative principles involved in each operation are primarily the same. The ingenuity, courage, and technical skill of the pioneers in the work are manifest to everyone reading their reports.

Sauvé, in an article on this whole problem published in 1908, stated that Mayo-Robson at the Congrès de Paris in 1900 credited Billroth with having removed the entire pancreas because of its involvement in a growth, with recovery of the patient; this was in 1884. Since no operative details of the case were available, however, Sauvé subtracted this case from his report. He included 8 other cases of resection of the head of the pancreas, those of Ruggi, 1889; Terrier, 1892; Kroen-

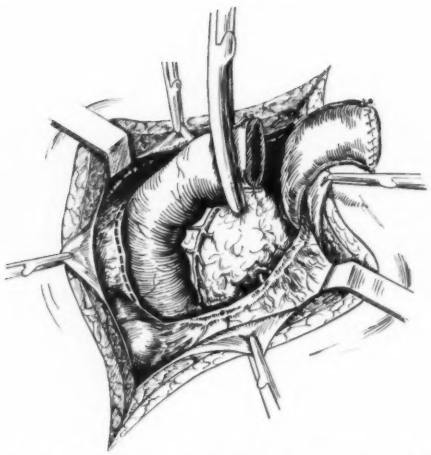


Fig. 2. Transection of duodenum between first and second portions. Mobilization of duodenum by incision along Wiart's line. (After Sauvé, *Rev. d. chir.*, 1908.)

lein, 1893; Biondi, 1896; Sendler, 1896; Tricomi, 1898; Codivilla, 1898; Franke, 1901. To these 8 he added 3 other cases, those of Tuffier, 1905; Michaux, 1906; and Duval, 1906. In 5 of these 11 patients an isolated benign tumor in the pancreas was resected; 3 of the patients recovered; and in 2 there was local resection of the pancreas for carcinoma; both patients died of metastases after 4 months. The 4 remaining patients had combined operations. Duval's patient was well 9 months after resection of the pyloric end of the stomach, which contained an ulcer perforating into the pancreas, resection of pancreatic tissue about the ulcer, and a posterior gastroenterostomy. Michaux removed the second and third portions of the duodenum with the contiguous pancreatic tissue, left the first portion of the duodenum together with the common duct intact, and performed an anterior gastroenterostomy; the patient died that same day of shock. Tuffier excised the head of the pancreas, ligating the common duct and performing a cholecystduodenostomy; the patient died 24 hours later. Codivilla performed a most interesting operation for which he is entitled to great credit. Finding a cancerous process in the head of the pancreas which could not be separated from the duodenum, he resected *en bloc* the head of the pancreas, a major portion of the duodenum and the pyloric end of the stomach, re-established the gastrointestinal flow with a Y-gastroenterostomy after the method of Roux, and with a Murphy button added a cholecystenterostomy. The patient lived for 24 days, dying with progressive cachexia and glycosuria.

The operative attack on growths situated directly at the papilla of Vater began in 1898 when Halsted, encountering a greatly dilated common duct and feeling a small hard growth at the ampulla, opened the duodenum, excised a V-shaped section of the duodenum, including the growth and the first portion of the common and pancreatic ducts, and closed the duodenum, implanting the stumps of both ducts into the suture line of closure. His patient lived free of symptoms for 7 months, then died with a recurrence of original growth.

Early in the operative story came the suggestion of a two stage operation, a suggestion which was founded on the belief that such obstructive symptoms as cholemia should be relieved by a less serious operation before radical extirpation of the tumor is attempted. Procedures of this sort were reported by Mayo in 1901 and Kausch in 1909; the former's first operation was a cholecystostomy, the latter's a cholecystenterostomy.

The two stage attack was likewise recommended by Sauvé in 1908 in describing an operation for resection of the head of the pancreas which he had conceived by dissection of fresh cadavers. At the first stage a gastroenterostomy was made, Sauvé calling this first stage "la reconaissance en force avant la bataille." He advised against forming the new path for the bile flow at this stage because this procedure would mask the operative field of the second stage. At the second stage the second portion of the duodenum together with the adjacent pancreatic tissue was resected and the bile flow was re-established by a choledochoenterostomy. Sauvé regarded this latter procedure as far preferable to a cholecystenterostomy or a cholecystgastrostomy since these two operations predisposed the patient to an angiocholitis of intestinal origin. Then Sauvé came to a prophetic conclusion when, in discussing the treatment of the remaining pancreatic

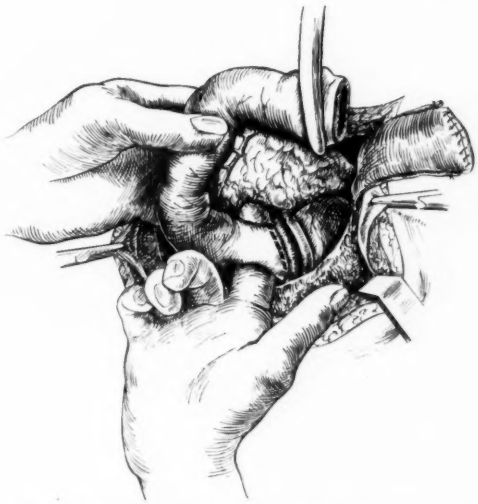


Fig. 3. Duodenum and head of pancreas freed. Superior mesenteric vessels isolated. (After Sauvé, *Rev. d. chir.*, 1908.)

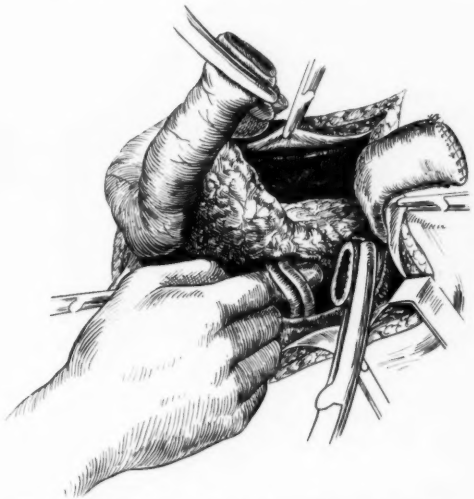


Fig. 4. Distal stump of duodenum brought out from under superior mesenteric vessels preparatory to closure of stump. (After Sauvé, *Rev. d. chir.*, 1908.)

stump, he pointed out the impossibility of suturing the duct of Wirsung directly to the intestine and condemned the attempt to graft the pancreatic stump into the intestinal canal. He ended the speculation about this problem by concluding that it is necessary to resign oneself to the loss of the external function of the pancreas. "Il faut donc se résigner á la perte de la fonction externe de la glande." As if such a departure seemed too radical, he added a last paragraph to say that to avoid fat necrosis it might be best to place drains down to the stump of the pancreas in order deliberately to form a pancreatic fistula (Figs. 2, 3, 4).

For the next 30 years no significant addition was made to the surgical treatment of lesions in the head of the pancreas or in the duodenum at the ampulla of Vater. Growths in the latter site, if attacked surgically, were treated by a transduodenal incision with a local removal after the manner of Halsted, although Koerte in 1904 tried a slightly more radical removal of the cancer by a circular resection of a small area of the duodenum just at the ampullary region, making an end-to-end anastomosis of the duodenum and implanting the common and pancreatic ducts into the suture line. His patient survived the operation only a few hours.

In 1905 Moynihan, in discussing operations for malignant disease of the pancreas, wrote: "I have elsewhere collected the records of all cases operated upon—13 in number. They all serve to show that the mechanical difficulties of the operation are well-nigh insuperable, and that if boldness and good fortune are the operator's gifts, the result to the patient hardly justifies the means."

Geiser in 1906 made a complete analysis of the subject of malignant disease of the duodenum, including all tumors of the ampulla of Vater, no matter what their histological origin, and collected 51 cases, of which 19 were operative, of what he called "periampullar" carcinoma.

To support the surgical attack on the pancreas, Coffey in 1909 devised in experimental animals an ingenious but rather complicated operation. He believed that the surgeon was fearful of operations involving the human pancreas because it was devoid of peritoneum, and that, although the fat splitting enzyme had been the dread of surgeons up to that time, there was no evidence that it would penetrate the peritoneum to a serious extent.

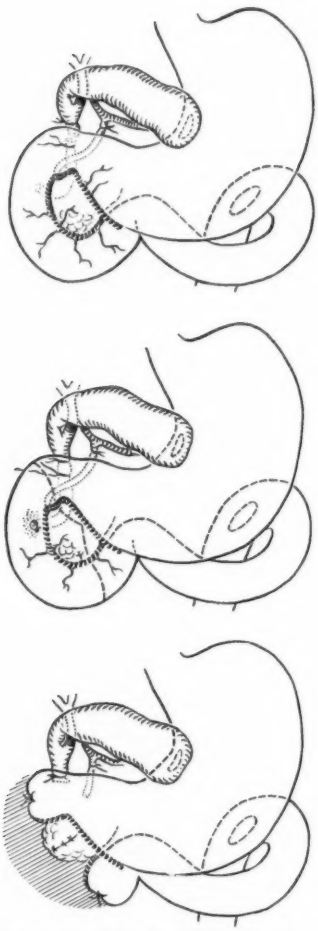


Fig. 5. Operation of Whipple, Parsons, and Mullins. 1935.

His was a two stage operation the scheme of which was to implant the stump of the pancreas into a loop of intestine, effecting a peritoneal covering for this stump by invaginating it into the intestine.

In 1913, after an extensive search of the literature, Outerbridge added 59 cases of periampullar carcinoma to the 51 Geiser reported, making a total of 110 available for analysis.

That the operative mortality continued high is borne out by the figures of successive investigators. In 1927 the report of Cohen and Colp of 59 cases of radical operations for carcinoma of the periampullary region represented their complete summary of the literature from 1898 to 1925, the operations being mostly transduodenal excisions with reimplantation of the common duct into the suture line, and some with reimplantation of the head of the pancreas into the duodenum. They reported a gross mortality of 43 per cent in 59 instances in which a variety of operative procedures was employed, and stressed the fact that even in two stage operations the risk of establishing external biliary drainage by some type of anastomosis between the biliary and upper intestinal tract in the presence of obstructive jaundice is not negligible, and that many patients subjected to such a procedure have not survived to undergo a radical excision of the growth.

In the same year, 1927, Fulde reported 52 operative cases with a mortality of 42 per cent. In 1931 Mueller and Rodemaker stated that the mortality rate of surgical procedures in this area was 30 to 70 per cent, depending on the duration of the jaundice and the type of operation performed.

In 1935 Whipple, Parsons, and Mullins added 20 reported cases to the 59 collected by Cohen and Colp, and described their two stage operation for carcinoma of the head of the pancreas. In 1935 also, Hunt and Budd collected 76 cases in which patients were treated surgically, including 18 cases between 1925 and 1934; the gross mortality was 39.77 per cent. In 1937 both Cooper and Brunschwig published reviews of the subject, and the latest report is by Kafka, a comprehensive review of all cases of periampullar carcinoma from 1900 to 1939. The results of operation in 115 patients are presented in Table I.

TABLE I.—RESULTS IN 115 CASES

	Excisions	Resections	Tota
Number of operations	94	21	115
Operative deaths	32	10	42
Per cent operative mortality	34	47.6	36.5

This brief review of the anatomy, the physiology, the clinical course of patients suffering from pathological conditions in this area, and the operative efforts to cure these conditions makes it clear why the region about the head of the pancreas has until now

been regarded by surgeons as a forbidden territory. The well conceived, if unsuccessful operation of Codivilla in 1898, the prophetic statement of Sauvé in 1908, and the successful operations reported by Whipple and his co-workers in 1935 have cut the Gordian knot which tied in fear the venturesome but conscientious operators for so many years. It now seems apparent that it is not necessary to attempt the hazardous procedure of re-establishing the flow of the external secretion of the pancreas into the intestine, and that a person may remain in good health without the digestive enzymes hitherto thought indispensable. There is, moreover, the possibility that the pancreas possesses, in addition to insulin, other internal secretions which aid in the metabolism of the fats and proteins and which are sufficient to maintain normal metabolism after all external secretions are blocked by ligation of the pancreatic ducts. This theory seems to coincide with the discovery of Dragstedt and his co-workers of a specific substance in alcoholic extracts of beef pancreas which on oral administration to depancreatized dogs treated with insulin permits survival and prevents the fatty degeneration and infiltration of the livers of these animals. This substance, for which the name "lipocaic" was suggested, is believed to be a new hormone that is concerned in some way with the normal transport and utilization of fat.

This same hypothetical internal secretion of the pancreas was thought by Boyce to explain the ability of dogs to digest an unusually high fat and protein diet after the exclusion of the pancreatic ducts from the intestinal tract but with the pancreas itself left undisturbed.

When, in 1935, Whipple, Parsons, and Mullins described their operative attack on carcinoma of the head of the pancreas they stimulated surgeons to new effort and revived flagging hopes. This operation was a radical excision *en bloc* of the tumor by a two stage procedure. In the first stage the patient was subjected to a gastrojejunostomy, ligation of the common duct, and cholecystgastrostomy; in the second stage, to an excision *en bloc* of the second portion of the duodenum including the ampulla of Vater, the lower common duct, and the surrounding portion of the head of the pancreas, with permanent ligation of the pancreatic duct and stump (Fig. 5).

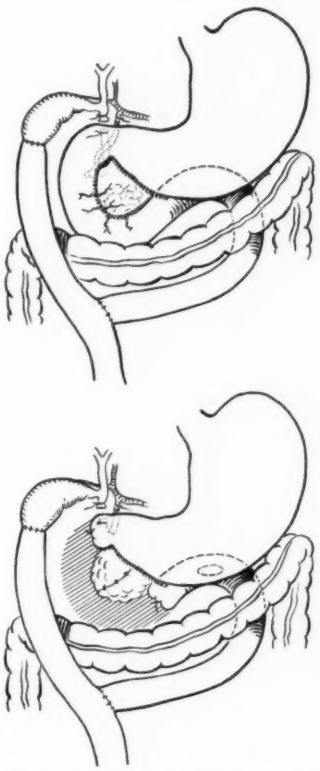


Fig. 6. Operation of Whipple. 1938.

This operation, although admirable in many ways, has certain objectionable features, some of which have already been eliminated by its authors. In the first place, an ascending cholangitis developed some months later in a number of patients subjected to this procedure, which was due apparently to the entrance of secretions from the stomach into the gall bladder directly through its line of anastomosis with the stomach. In 1908 Sauvé, as stated before, made this observation and maintained that there would be less danger of retrobiliary inflammation if the gall bladder or the common duct was anastomosed to the duodenum or to the jejunum

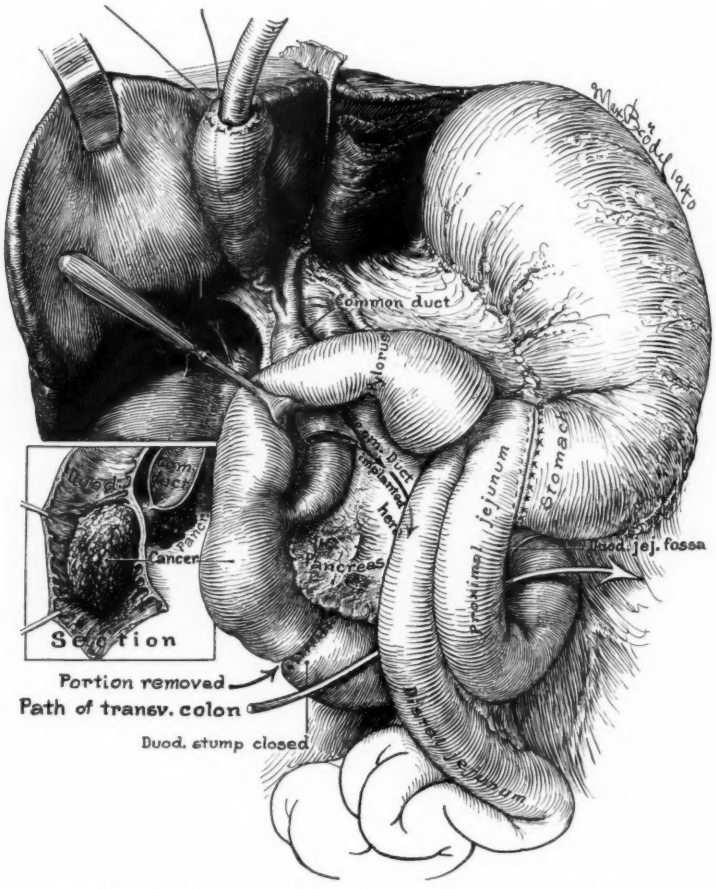


Fig. 7. This shows the resection of the duodenum, the pyloric end of the stomach, the common duct, and the head of the pancreas. It also shows the anterior Pólya anastomosis, the transverse colon being omitted from the drawing for the sake of clearness.

instead of to the stomach. Brunschwig in 1937 was the first to use a loop of jejunum for the gall-bladder anastomosis, with a side-to-side jejunojejunostomy in the first stage of the operation. In 1938 Whipple and his associates changed their procedure so that now the first stage consists of a ligation of the common duct, and an antecolic cholecyst-jejunostomy on the Roux principle of anastomosing the distal cut end of the jejunum to the fundus of the gall bladder, with an end-to-side anastomosis of the proximal cut end of the jejunum to the side of the jejunum 10 to 12 centimeters below the cholecystenterostomy. In the second stage of the operation the patient was subjected to a gastrojejunostomy, followed by excision of descending portion of duodenum and ampulla of Vater, lower end of common duct, and wedge-shaped portion of head of the pancreas, with ligation of cut end of pancreatic duct and closure of pancreatic stump (Fig. 6).

Another objectionable feature in the operation as previously performed was the frequent development of a biliary fistula from the ligated stump of the common duct. In all

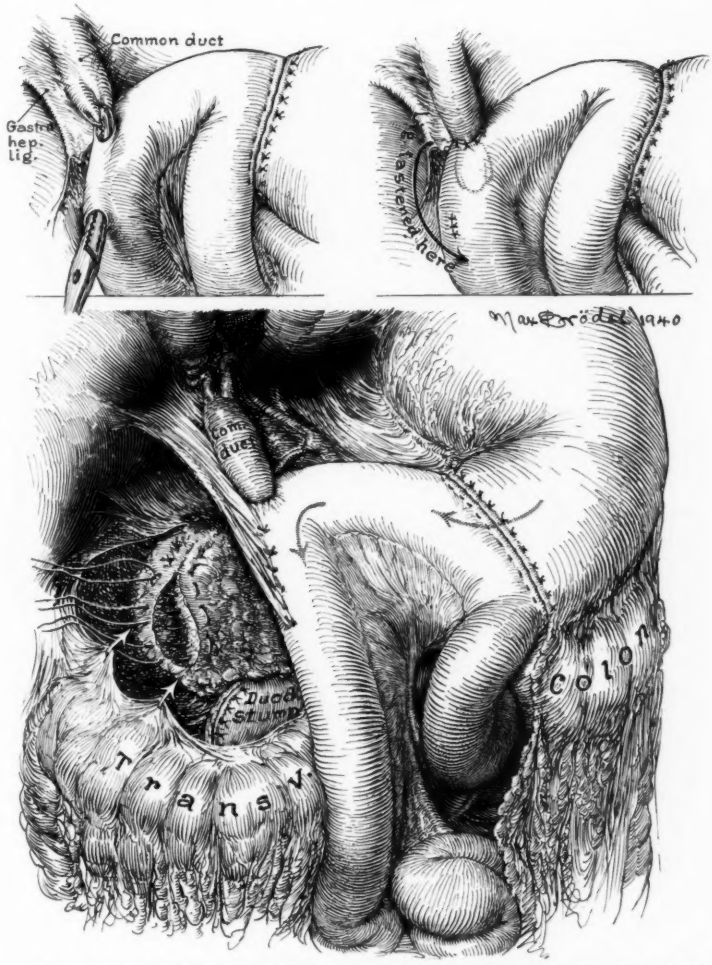


Fig. 8. This shows the suture of the pancreatic stump, including the pancreatic ducts, and the implantation of the stump of the common duct into the jejunum.

probability this is due to necrosis of the thin walled avascular common duct at the point of ligature, which is also the cause of the temporary leakage of small amounts of bile around the cigarette drain inserted down to the ligated stump of the cystic duct after the usual cholecystectomy. In our operation we avoided this complication because, instead of leaving a ligated blind stump of the common duct, we anastomosed the open end of the common duct directly to the intestinal tract.

One other objection which may be raised to resections in this area, as previously carried out, is that, whereas the second portion of the duodenum was resected, the first was left in place closed over as a blind stump, and the patency of the gastrointestinal tract was restored by a gastroenterostomy. This proximal duodenal stump forms an additional suture line and, therefore, an additional potential point of leakage. We have avoided this difficulty by resecting the entire first

portion of the duodenum as well as the second portion and also the pyloric end of the stomach, and by restoring the gastrointestinal flow by one suture line only, an end-to-side anastomosis between the jejunum and the distal end of the stomach, the so called anterior Pólya anastomosis. This procedure has the additional great advantage of bringing the jejunum high up under the edge of the liver where the stump of the common duct may be anastomosed to it without tension.

A final objectionable feature to the operation as previously carried out arose from its performance in two stages, and this objection we have attempted to eliminate by our single stage attack. Many times after the performance of the first stage of a planned two stage operation, the patient, greatly improved by the re-establishment of the biliary flow, is lulled into a sense of false security and is unwilling to undergo the second operation. The chief argument of the proponents of a two stage procedure is the restoration of the flow of the bile into the intestinal tract by the first operation, thus enabling the patient better to withstand the subsequent resection, with less tendency to hemorrhagic manifestations so common to all forms of obstructive jaundice. This seems a reasonable tenet, particularly in very ill or in elderly patients in whom a two stage performance of an operation may prevent the whole of the operative shock from equalling the sum of all its parts. However, the present use of vitamin K has reduced the hazard of hemorrhage, thereby rendering some of these very ill patients justifiable risks for an operative procedure in one stage. The chief advantage of a one stage performance is that all the work is done in a clean operative field as opposed to a field masked and obscured by trauma of a preliminary operation. With so many vital structures in so small a space, complete differentiation is difficult but imperative in order to avoid injury to these structures and to effect the delicate restorative anastomoses. Many times at the second operation in a two stage performance the adhesions are so dense that removal of the growth at the head of the pancreas is found impossible. We believe, therefore, that the excision of a carcinoma situated in this region will be attended with the greatest chance of success if the operation can be done in one stage after the patient has received proper vitamin therapy and is given a large transfusion at the very beginning of the operation, which is allowed to run continuously during entire course of the operation.

CASE REPORT

M. McF., a white woman, aged 42 years, complained of severe pain beneath the lower end of the sternum, fever, and jaundice. Her father was alive but suffered with diabetes. She had always had excellent health.

In September, 1939, an attack of intense pruritus developed which continued 11 weeks; it was not accompanied by jaundice or any other symptom. Following the subsidence of this attack, about the middle of December, 1939, she was well until March, 1940, when the pruritus returned and was soon followed by an obstructive type of jaundice, but no pain. She was a patient in the Johns Hopkins Hospital for a period of 2 weeks at this time, from March 23, 1940, to April 6, 1940, when on examination she was found to be physically sound except for the jaundice and an enlarged left kidney. The blood count showed a microcytic, hyperchromic anemia. The red blood cells numbered 4,420,000, the hemoglobin was 9.3 grams (64 per cent), and the white blood cells, 5,580. The blood analysis showed cholesterol 417 milligrams per cent, sugar 91 milligrams per cent, nonprotein nitrogen 34 milligrams per cent, and the van den Bergh a delayed biphasic reaction, 2.0 milligrams per cent. The stools were clay-colored and gave a positive guaiac and benzidine reaction. The urine was deeply pigmented by bile. Roentgenograms of the stomach and gastrointestinal tract revealed no abnormality; those of the gall bladder showed failure to concentrate the dye. The jaundice diminished while she was in the hospital and she was discharged untreated April 6, 1940, with the diagnosis of catarrhal jaundice.

Following her return home the itching and jaundice persisted. Suddenly in the morning of April 25, 1940, she had sudden severe pain high up in the epigastrium running up beneath the sternum, was nauseated, and vomited. The pain remained severe. She was seen that same afternoon in consultation at the request of Dr. John W. Parsons and admitted to the Church Home and Infirmary.

Examination showed a well developed, well nourished woman of 42 years who was suffering with abdominal pain. The temperature was 100.6 degrees, the respirations were 18, and the pulse was 90. There was a definite icteric tint to the skin and sclerae. The lymph glands were not enlarged. The lungs were clear. There was a loud systolic murmur at the apex of the heart. The abdomen showed restricted motion in the right upper quadrant where there was some tenderness and muscle spasm, but

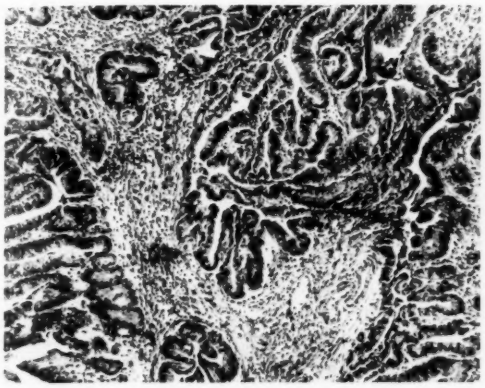


Fig. 9. Papillary carcinomatous growth invading wall of duodenum.

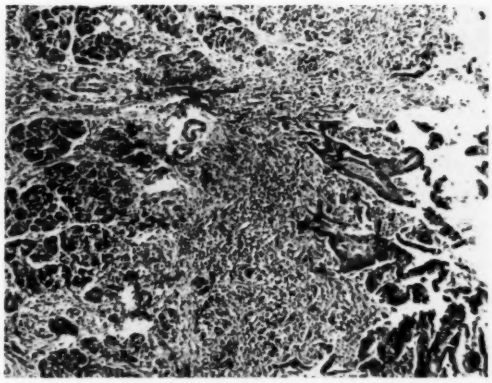


Fig. 10. Junction of normal pancreatic tissue (left) and carcinomatous tissue from ampullary area of duodenum (right).

no definite mass could be felt here. The blood showed 28,000 white blood cells; hemoglobin, 82 per cent; icteric index, 30; and Kahn test, negative. The urine was deeply pigmented with bile but showed no sugar or albumin; the voided specimen contained a few red and a few white blood corpuscles (the patient was menstruating).

On April 26, 1940, the day after admission to the hospital, since her temperature had risen to 103 degrees, and since the abdominal symptoms had not abated, after consultation with Drs. J. W. Parsons and W. A. Baetjer, she was subjected to operation. A needle was introduced into the antecubital vein of the left arm and a 5 per cent dextrose solution in normal saline was allowed to run slowly during the entire course of the operation. Anesthesia was induced with nitrous oxide and oxygen and continued with drip ether on the open mask by Dr. S. Griffith Davis. Through a high right rectus incision an enlarged, tense, smooth walled gall bladder was found that could not be emptied by pressure. The cystic duct was very small. The common bile duct was greatly dilated, measuring 1.5 centimeters in diameter; seropurulent fluid was aspirated from this duct and Gram positive diplococci were found on smear. No stones could be palpated in either the gall bladder or the common duct. A soft round tumor mass could be felt within the second portion of the duodenum. Through a small longitudinal incision in the duodenum this mass was seen to be a papillary growth 3 centimeters in diameter surrounding the ampulla of Vater which by frozen section proved to be adenocarcinoma.

It was decided to resect this growth with its duodenal, choledochal, and pancreatic connections. The duodenum was mobilized and divided between clamps at the distal end of its second portion. The resected duodenum was reflected to the right, the head of the pancreas removed with it, and in the same block the distal 5 centimeters of the stomach. The first and second portions of the duodenum together with the pyloric portion of the stomach, the distal end of the common duct, and the head of the pancreas were then resected *en masse*. All bleeding points were ligated, catgut being used because of the organisms found in the material aspirated from the common duct. The cut surface of the pancreas was transfixed with mattress stitches of catgut. The distal stump of the duodenum was turned in with a continuous double row of No. 0 chromic catgut, and this closure was reinforced with a layer of mattress sutures of fine silk. A loop of jejunum about 30 centimeters from Treitz' ligament was brought anterior to the transverse colon and sutured to the open stump of the stomach, after the anterior Pólya method. The stump of the common duct was implanted into the side of the jejunum about 20 centimeters distal to the site of the gastrojejunostomy. This step was accomplished by first making a small incision in the jejunum distal to the proposed site of implantation, placing a Kelly clamp within the bowel and out through the jejunum at the proposed site, drawing the stump of the common duct into the duodenum, and suturing the duct to the proximal opening in the jejunum with interrupted stitches of fine silk. This procedure was effected only after some difficulty because of the extreme thinness of the walls of the common duct. The line of anastomosis was reinforced by stitching omentum about the suture line. The distal opening into the jejunum was closed with interrupted silk stitches. One cigarette drain was inserted into the lesser peritoneal cavity and one placed down to the anastomosis between the common duct and the jejunum. The deeper layers of the wound were closed with catgut and the skin was closed with silk. The patient received 500 cubic centimeters of blood during the latter part of the operation through the intravenous cannula already in place. She withstood the long procedure very well; at the close of the operation the pulse was regular at 120 beats a minute and blood pressure was 110/75 (Figs. 7, 8, 9, 10).

The patient recovered rapidly from the operation. There was no vomiting, no pancreatic or biliary drainage after the first few days, and no digestive discomfort or fatty stools. Pancreatic enzymes given by mouth proved distasteful and were stopped. On the sixteenth postoperative day she suffered a rather severe hemorrhage of undetermined origin, vomiting blood and losing some blood from the abdominal wound. Thanks to the alertness of Dr. Howard Jones and his staff at the Church Home and Infirmary she received a transfusion within a few minutes after the onset of the hemorrhage. After that she improved rapidly and was discharged from the hospital on June 2, 1940, 5 weeks after operation.

She returned a month later to her position as secretary and stenographer, where she works 8 hours a day. She has gained 15 pounds. There has been no digestive disturbance except once or twice a transient vague epigastric discomfort after eating the fat in ham, and no abnormality in the stools. These are well formed and of a normal consistency and color, showing no evidence at any time of steatorrhea. Serum lipase estimation was made on January 8, 1941, 9 months after operation, after the method of Comfort and Osterberg, and found to be 1.41, expressed in cubic centimeters of twentieth normal sodium hydroxide solution. The serum diastase was determined on the same date by the glycogen cleavage method, expressed in cubic centimeters of thiosulphate solution required in the titration of the maltose formed by incubating the serum with 1 per cent glycogen solution. This was 0.745 cubic centimeters. These two determinations are believed to be within the limits of normal.

In answer to a letter which we wrote to Dr. A. O. Whipple on October 22, 1940, telling him of our patient who was subjected to operation on April 26, 1940, he sent a very courteous reply describing 2 patients of his in which much the same operation as ours was employed. The first patient was operated on by him on March 6, 1940, and is in excellent health except for the necessity of taking pancreatic extract to avoid the loss of too much fat in her stools. His second one stage procedure was done in October, 1940, the patient died in 6 days of an overwhelming lobar pneumonia.

SUMMARY

1. The difficulties of a surgical attack upon the ampullary region of the duodenum and the head of the pancreas are outlined.

2. A brief survey of the operative story is given.

3. A one stage operation for the cure of carcinoma in this area is described together with a clinical report of the case.

4. In this patient the deprivation of the pancreatic secretion by permanent ligation of the pancreatic duct has for the past 11 months had no apparent effect upon the digestion of fat, carbohydrate, and protein.

REFERENCES

1. Billroth, T. Quoted by Oser, L. Loc. cit.
2. Biondi, A. Cited by Sauvé, L. Loc. cit. (33).
3. Boyce, F. F., and McFetridge, E. M. Surgery, 1938, 4: 51–63.
4. Brunschwig, A. Surg., Gynec. & Obst., 1937, 65: 681–684.
5. Codivilla, A. Cited by Sauvé, L. Loc. cit. (34).
6. Coffey, R. C. Ann. Surg., 1909, 50: 1238–1264.
7. Cohen, I., and Colp, R. Surg., Gynec. & Obst., 1927, 45: 332–346.
8. Cooper, W. A. Ann. Surg., 1937, 106: 1009–1034.
9. Dragstedt, L. R., Van Proheska, J., and Herman, P. H. Am. J. Physiol., 1936, 117: 175–181.
10. Franke, A. Arch. f. klin. Chir., 1901, 64: 364–392.
11. Fulde, E. Zentralbl. f. Chir., 1927, 54: 1481–1487.
12. Garrison, F. H. History of Medicine. 4th ed. Philadelphia and London: W. B. Saunders, 1929.
13. Geiser, J. F. Deutsche Ztschr. f. Chir., 1906, 86: 41–107.
14. Halsted, W. S. Boston M. & S. J., 1899, 141: 645–654.
15. Idem. Johns Hopkins Hosp. Bull., 1901, 11: 1–11.
16. Howell, W. H. Text Book of Physiology. 12th ed. Philadelphia and London. W. B. Saunders, 1933.
17. Hunt, V. C., and Budd, J. W. Surg., Gynec. & Obst., 1935, 61: 651–661.
18. Judd, E. S., and Hoerner, M. T. Arch. Surg., 1935, 31: 937–942.
19. Kafka, W. Beitr. z. klin. Chir., 1939, 170: 547–559.
20. Kausch, W. Zentralbl. f. Chir., 1909, 36: 1350–1353.
21. Koerte, W. Beitr. z. Chir. der Gall. u. der Leber, Berlin, 1905, 224.
22. Kroenlein, R. U. Beitr. z. klin. Chir., 1895, 14: 663–696.
23. Moynihan, B. G. A. Abdominal Operations. Philadelphia and London: W. B Saunders, 1905, 633.
24. Mayo, W. J. St. Paul M. J., 1901, 3: 374.
25. Idem. Ann. Surg., 1906, 44: 209–216.
26. Mayo-Robson, A. W. 13th Congrès Int. de Méd., Paris, 1900.
27. Mueller, G. P., and Rodemaker, L. Ann. Surg., 1931, 93: 755–760.
28. Nimier, H. Rev. de chir., 1893, 13: 1016–1019.
29. Oser, L. Die Erkrankungen des Pankreas, Vienna, 1898.
30. Outerbridge, G. W. Ann. Surg., 1913, 57: 402–426.
31. Ruggi, G. Cited by Nimier, H. Loc. cit.
32. Santorini, G. D. Observationes Anatomicae, Venice, 1724. Cited by Garrison, F. H. Loc. cit.
33. Sauvé, L. Clin. chir., 1896, 4: 131–145.
34. Idem. Rend. stat. sez. chir. osp. di Imola, 1898.
35. Idem. Riforma med., 1898, 14: 433–437.
36. Idem. Rev. de chir., 1908, 37: 335–385.
37. Sendler, P. Deutsche Ztschr. f. Chir., 1896, 44: 329–345.
38. Terrier, F. Cited by Nimier, H. Loc. cit. (29).
39. Tricomi, E. Cited by Sauvé, L. Loc. cit. (35).
40. Upcott, H. Ann. Surg., 1912, 56: 710–725.
41. Vater, A. Dissertatio anatomica qua novum bilis diverticulum circum orificium ductus choledochi. Wittenberg, 1720.
42. Whipple, A. O. Am. J. Surg., 1938, 40: 260–263.
43. Whipple, A. O., Parsons, W. B., and Mullins, C. R Ann. Surg., 1935, 102: 763–779.
44. Wirsung, G. Padua, 1642. Cited by Garrison, F. H Loc. cit.

SLIPPING OF THE UPPER FEMORAL EPIPHYSIS

M. BECKETT HOWORTH, M.D., Sc.D. (Med.), F.A.C.S., New York, New York

NO altogether satisfactory name has been devised to include all phases of this disease. The terms epiphyseolisthesis and epiphyseolysis are perhaps suitable for expressing the condition of the epiphyseal disc at two stages, but do not include the earliest and latest stages nor the changes in the soft tissues. The terms preslipping or slipping of the upper femoral epiphysis will be used here for the sake of convenience.

A study of 70 cases of this condition from the New York Orthopaedic Hospital was presented 8 years ago.[1] Sixty-two additional patients have been treated since that time, a total of 132. The statements made in the present report are based upon a careful and complete analysis of all of these cases seen personally. Detailed statistics and tables will be omitted, but are available.

ETIOLOGY

The incidence was slightly greater in boys than in girls, possibly due to the greater activity of the adolescent boy. The condition was bilateral in one-fifth of the first group but in only one-fifteenth of the second. This difference is probably explained by the earlier diagnosis in the latter group, with attendant protection of the second hip. The right hip was involved in 38 per cent, the left in 48 per cent, while 14 per cent were bilateral. Only half of the children were of the endocrine type, but 65 per cent were tall or overweight. It is difficult to explain this disease on a purely endocrine basis as at least half of the children were not of the endocrine type, and it is preponderantly unilateral. Tonsils had been removed at, or shortly before, onset in half of the cases, and other foci of infection were present in 20 per cent. Trauma of sufficient degree to cause an epiphyseal displacement was rarely present. Trauma was absent at the onset of most of the cases, and when present was usually trivial, such as stepping off the curb. Frequently the patient dates the onset from some minor injury, but in almost every case there were symptoms before the injury. It is certain that trauma is not the primary cause of the disease, but rather a frequent incident in its course.

STAGES

There are four stages of the disease, although there often may be no sharp division between them. They are the preslipping, slipping, quiescent, and residual stages. The existence of the *preslipping* stage has been denied, but there is abundant evidence to support its existence. It may not be seen when the child does not seek early medical care, or when this stage is not recognized by the physician. Nineteen of these cases had definite symptoms, signs, roentgenographic changes without evidence of slipping in anteroposterior and lateral roentgenograms, and pathological changes upon exposure of the hip at operation. Slipping subsequently occurred in 2 of them, whereas in the others the evidences of disease disappeared after operation. The *slipping* stage may begin suddenly or gradually, and the slipping may continue for several months. The condition is *quiescent* when the symptoms and signs have subsided and the roentgenogram shows a healed epiphyseal line. It is *residual* when there is complete bony union at the line.

ONSET

The age at onset of the preslipping stage was 9 to 16 years, the average 12 years. The onset averaged 18 months earlier for girls than boys. The age at slipping was 10 to 17 except in 2 frankly traumatic cases, aged 8 and 9 years. The average age for slipping was 13.5 years. The age for slipping was 2 years younger for girls than boys. The interval between onset and slipping averaged 1 year, and the interval tended to be shorter in the older children.

From the New York Orthopaedic Dispensary and Hospital.

[1] J. Am. M. Ass., 1931, 97: 1867.

PRESLIPPING STAGE

The onset of the preslipping stage is usually gradual and vague. Every patient complained of a limp or pain, and most of them mentioned both. Usually there was some disability for vigorous activities, such as athletics. A minority noticed limitation of motion, weakness, and easy fatigability. The limp was also noticed upon examination, and varied in degree and protectiveness. Internal rotation, adduction, and often flexion were almost always found to be slightly limited, with pain and spasm at the extremes. The other motions were occasionally limited. The motions are grouped together for simplicity, and an index used expressing approximately the total percentage. An index of 90 to 110 represents normal motion. The index of motion in these cases ranged from 65 to 100, averaging 77. Slight atrophy of the thigh was common.

The leucocyte count of the blood was ten to twelve thousand in half of the cases, but the polymorphonuclear percentage was not increased. The erythrocyte sedimentation rate was above 10 in 90 per cent of the cases, and as high as 40, averaging 25 millimeters. Tests for syphilis and tuberculosis were uniformly negative.

The roentgenographic features were widening and irregularity of the epiphyseal line, with decalcification of the proximal end of the neck. The head was not visibly affected. The capsule was usually swollen.

SLIPPING STAGE

In some cases there is a sudden slip, accompanied by aggravation of symptoms and signs. In extreme cases the patient is unable to bear weight on the hip, and has severe pain, spasm, and limitation of motion. The slipping is so gradual in other cases that no change is noted in the symptoms.

The roentgenogram reveals the degree of slipping. The typical deformity is a downward and backward displacement of the head with adduction (varus). There is only the posterior displacement in some cases, while in others the downward displacement is much greater than the posterior. The degree of posterior displacement may best be seen in the lateral view. Callus forms in the inferior and posterior interval between the head and neck and may be seen soon after the slip. In many cases two or more layers of callus may be seen, indicating that two or more slips have occurred.

As the lesion becomes quiescent in either the preslipping or slipping stage, the epiphyseal line begins to assume its normal width and regularity, and the proximal end of the neck recalcifies. The callus soon becomes mature. The proximal margin of the neck superiorly loses its angular appearance and becomes smooth and level with the head. In younger children this smoothing and leveling of the neck may go so far as almost to obliterate the deformity of the slipping, leaving only a coxa vara. After several months or years, depending upon the age of the patient, the epiphyseal line becomes ossified, thus reaching the residual stage at about the age of 16 in girls, 18 in boys. When there is much displacement, arthritic lipping at the margin of the head usually supervenes, and later it may involve the acetabulum. Downward displacement of the head is more serious than a posterior one in producing limitation of motion and arthritic changes. Circulatory changes in the head are rarely seen when the head has not been separated from the neck by surgical means.

PATHOLOGY

We have operated upon 17 hips in the preslipping stage and 53 which have slipped, at varying degrees and periods after slipping, a total of 70 hips. Thus there has been an opportunity to study at first hand the pathology of the soft tissues of these hips. There are in the literature a few reports of examinations of the femoral head and neck at autopsy or resection late in the disease. Reports of the pathology of the soft tissues are essentially lacking. In the preslipping stage the capsule was usually found to be edematous and thickened, the periosteum of the neck and the synovial membrane were almost always thick, red, softened, and vascular, with a tendency toward pannus formation. The synovia was often increased in amount. The cartilage of the head and bone of the neck were normal

except for an occasional granular appearance at the junction. Often the softening of the epiphyseal disc could be felt with the instrument. Microscopic examination usually revealed edema and hypervascularity of the synovial membrane, with collections of small round cells about the small blood vessels. Cultures of the synovia and the soft tissues were consistently negative in all stages.

The soft tissues in those patients seen after slipping, presented an appearance similar to that of the preslipping stage. There was usually a fold of soft redundant synovial membrane in the angle inferiorly and posteriorly, and an early pannus. The displacement of the head on the neck could also be seen, but not even in those patients seen within a few days of slipping was there separation of the head and neck. There was always a layer of firm fibrous or cartilaginous tissue covering the exposed portion of the end of the neck and joining it to the cartilage of the head. There was usually firm union of the head to the posterior-inferior portion of the end of the neck. Usually the distal side of the epiphyseal disc was soft, but in the later stages it had become firm again, sometimes solidly ossified. The cartilage of the epiphyseal disc had in most cases almost entirely disappeared, but the adjacent layer of capital cortex appeared normal. It appeared probable that in some cases there was no sudden slip, but a gradual displacement through the plastic tissue at the junction of the neck with the epiphyseal disc. Callus in various stages of maturity usually filled the angle inferiorly and posteriorly between the head and neck. Microscopic examination soon after a slip showed a thickened, vascular and edematous synovial membrane similar to that of the preslipping stage. The membrane in the later cases was thickened, but sclerotic and somewhat vascular.

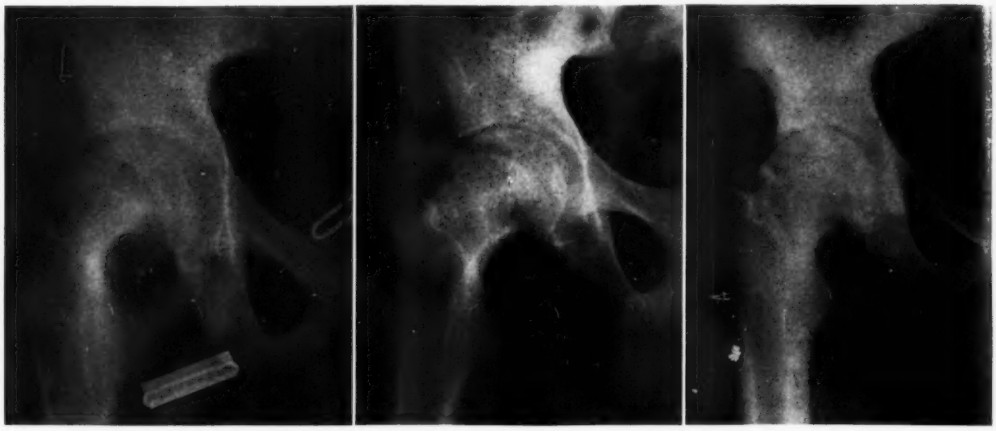
THEORY OF CAUSE

What is the cause of this condition? Is the slipping primary or does it follow a softening and weakening at the epiphyseal line? The disease is seen only in children between the ninth and eighteenth years, which is the period of rapid growth. Many of the children are overweight or overgrown. The epiphysis appears to be normal previous to the onset of symptoms. The early symptoms and signs are those of a synovitis, and a swollen capsule is found in the roentgenogram. The sedimentation rate is usually elevated. The gross and microscopic pathology is that of a mild synovitis. We have seen 19 cases with these findings before any slip occurred. It appears that the primary condition is a synovitis of the hip during the period of rapid growth, and that this lesion causes circulatory changes in the epiphyseal disc resulting in decalcification and softening. The slipping is merely the natural result of weight bearing or mild injury to the softened epiphyseal junction. The cause of the synovitis is not proved, though the clinical and pathological picture and the elevated sedimentation rate suggest infection. The negative cultures may be due to our technical inability to culture the organism or virus involved, or the failure to take the culture early enough.

RESULTS

Methods of evaluation. Our purpose in the treatment of this condition is to secure a painless hip free of limp, with full motion and full capacity for normal activity. Hence our results must be evaluated in terms of the normal hip symptomatically, functionally, and anatomically, on a long term basis. The motions are grouped together for simplicity in a formula which approximates percentage. Further, we must know the results in untreated hips for comparison with treated ones. We should also know the relation of deformity to function, the effect of the impingement of the exposed neck on the acetabulum, and the importance of changes in the head due to circulatory disturbance. Finally, osteoarthritis in the residual stage must be considered. Untreated patients often get good hips even with moderate deformity, and they do not get the secondary changes in the head which often follow reduction. The lesion always heals and the patient can eventually walk, regardless of treatment. Our evaluation must be much more exact. We shall consider the results in the various stages in reverse order.

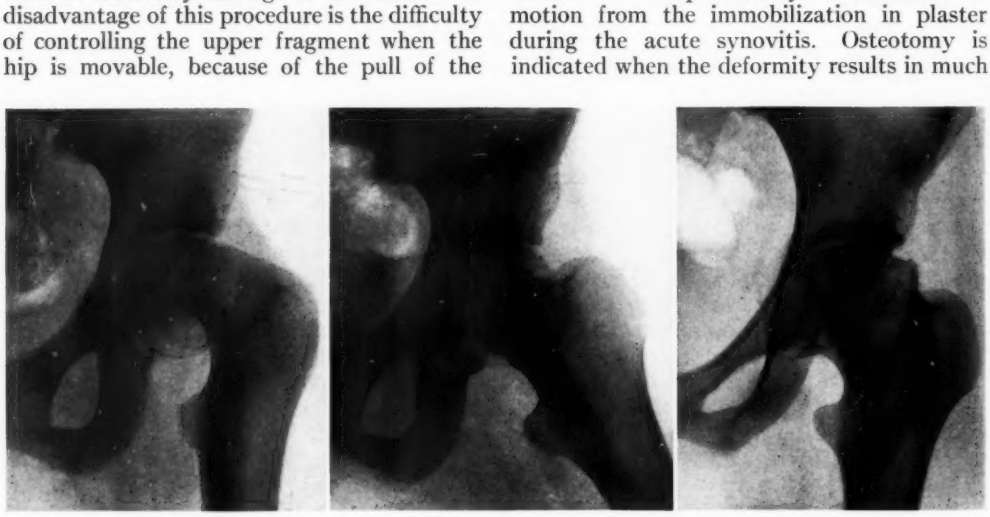
Treatment in quiescent and residual stages. Correction of deformity is usually the



a b c

Fig. 1. Male, aged 14 years. a, Symptoms 1 month; head displaced downward ¾ inch, moderately posteriorly; index of motion, 17. b, After reduction by strong traction. Double spica in abduction and internal rotation for 3 months. c, Roentgenogram which was taken 9 years after reduction. This is the best hip which was reduced by strong traction; index of motion, 66; little deformity is present.

chief problem in these stages. This may be accomplished by osteotomy through the healed epiphyseal disc, through the neck, or below the trochanters. Subtrochanteric osteotomy is preferred, because there is less likelihood of secondary damage to the head. The disadvantage of this procedure is the difficulty of controlling the upper fragment when the hip is movable, because of the pull of the psoas muscle. We have used the operation in 6 cases with fairly satisfactory results. This operation may sometimes be preferred to open reduction soon after slipping. It should, however, be postponed to the quiescent stage because of the probability of limitation of motion from the immobilization in plaster during the acute synovitis. Osteotomy is indicated when the deformity results in much



a b c

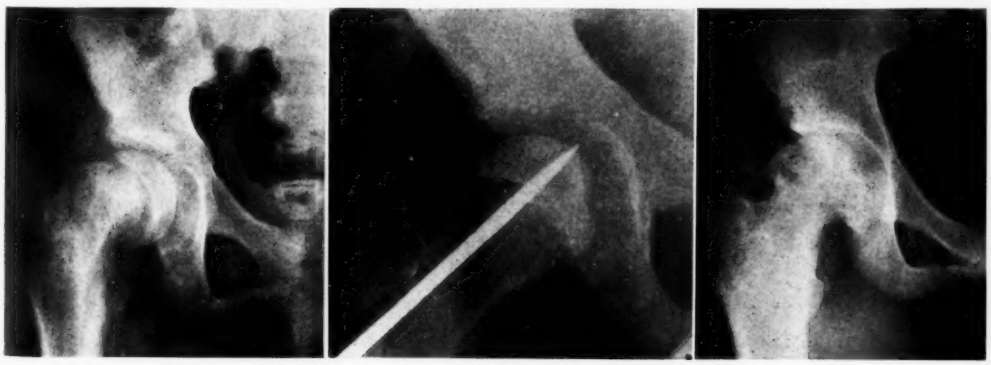
Fig. 2. Female, aged 14 years. a, Symptoms 8 months; index of motion, 11; head displaced downward, ¾ inch and posteriorly; joint space thin; open reduction August 31, 1932. b, After removal of spica, 12 weeks after operation. c, Head degenerated 3 years after operation; 7½ years after operation, index of motion, 13.

a b c

Fig. 3. Male, aged 14 years. a, Symptoms 5 months, sudden increase 3 days previously; callus in inferior angle; head displaced downward ¾ inch, moderately posteriorly; index of motion, 20. b, Three months after open reduction and nailing; slight overreduction (intentional). c, Roentgenogram of the same hip which was taken 1 year after operation; no pain; view 5 years after operation; index of motion was 66.

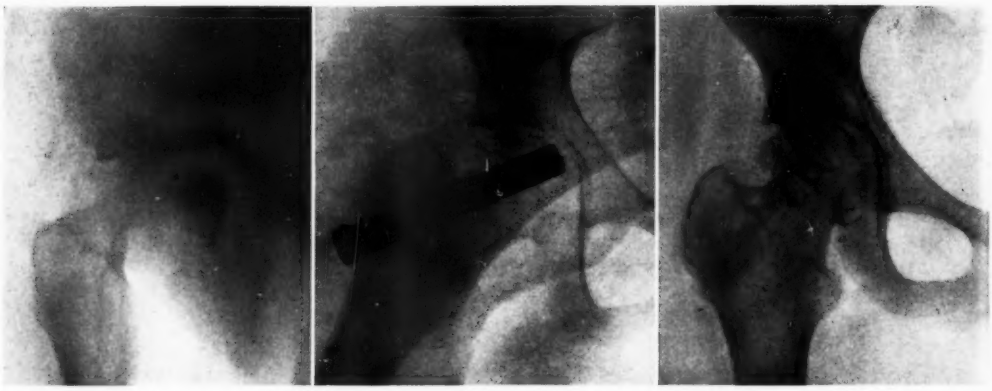
limitation of motion (usually abduction and internal rotation) and when there is impingement of the neck against the acetabulum with the resultant tendency to arthritis.

Treatment in slipping stage. It is desirable to reduce the deformity when there is one-half inch or more of displacement downward or posteriorly. We have attempted to reduce these deformities when the lesion had not already reached the quiescent stage. It was found in the first study that closed reduction by manipulation into abduction and internal rotation was unsatisfactory. Partial reduction was obtained in only 3 of 21 cases. These 3 reductions were done shortly after the slip, with no callus in the inferior angle. Only one additional closed reduction has been attempted in the past 10 years, and this resulted in little correction. Most of these hips had some permanent limitation of motion due to the immobilization, and there were occasional circulatory changes in the head, due to tension on the capsule. Better results could probably have been obtained with bed rest alone until



a b c

Fig. 4. Male, aged 13 years. a, Symptoms 2 weeks; reduced with Russell traction. Allowed up at 8 weeks and slipped again more than at first. Index of motion, 25. b, Open reduction and nailing. Good reduction. Suspension and traction for 6 weeks. Nail removed at 7 weeks. Index of motion, 46. c, Two years after operation. Fully active without symptoms; no deformity; index of motion, 90. The best result with open operation.

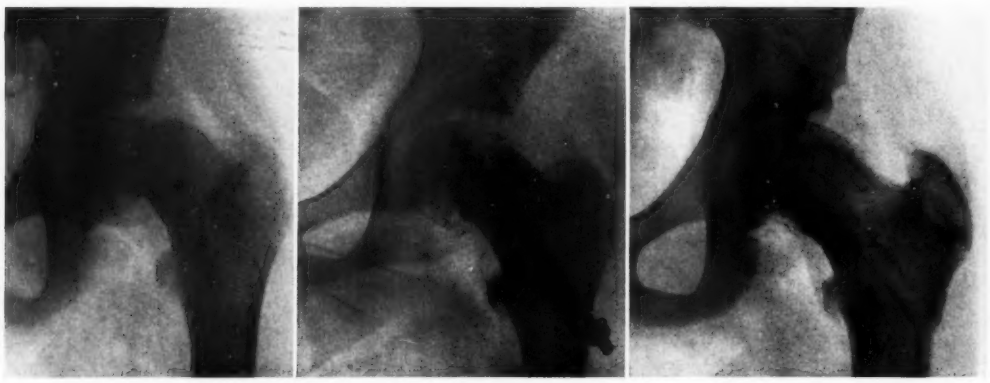


a b c

Fig. 5. Female, aged 12 years. a, Symptoms 2 months. Index of motion, 10; head displaced downward 1 inch, and posteriorly, with neck impinging against acetabulum. b, January 3, 1936, open reduction and fixation with Smith-Petersen nail. Motion begun first week, nail removed 8 weeks after operation. c, Roentgenogram of same hip which was taken 8 months after operation. Index of motion at one year was 36.

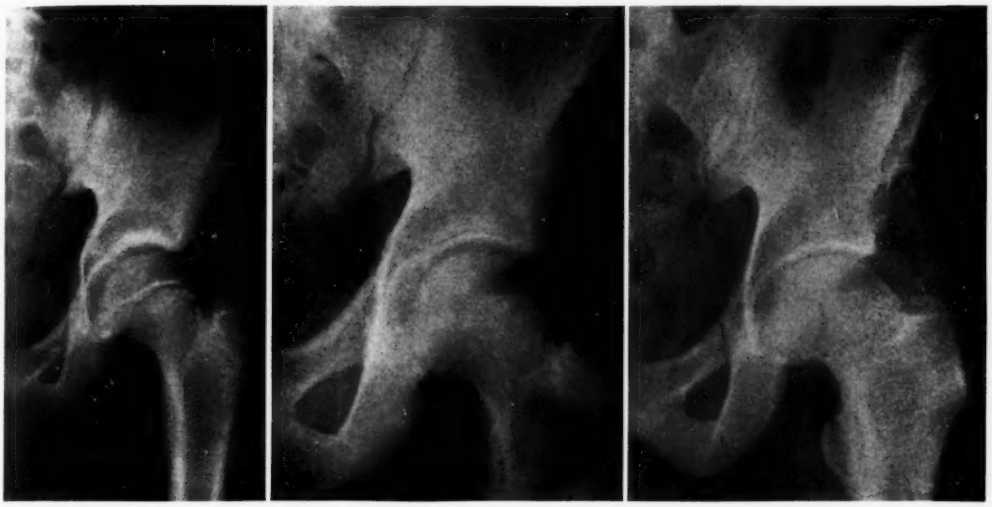
the condition became quiescent, possibly followed by subtrochanteric osteotomy. This procedure is advised only for recent slips with no callus inferiorly, and nailing might be preferable to plaster immobilization.

Reduction by strong traction. Nine years ago we reduced 7 epiphyses by very strong traction followed by internal rotation, and immobilized them in plaster in abduction and internal rotation. The downward displacement was corrected in most of them. Usually the rotation could not be corrected. All of the epiphyseal discs healed well, but in most of the hips the cortex of the head became irregular, and in some cases irregularly ossified and the joint space thin. Eventual motion was good in only one hip (Fig. 1), fair in one, and poor in the others. This was probably due to injury to the capsule and the circulation by the traction and the tension in plaster. The results would probably have been better had bed rest alone been used until the lesion healed, possibly followed by subtrochanteric osteotomy. Probably nailing such hips after



a b c

Fig. 6. Male, aged 15 years. a, Symptoms 1 year. Callus in inferior angle. Head displaced downward ¾ inch, moderately posteriorly. Index of motion, 90. b, After open reduction and Lippman screw. Fair reduction. c, Thirteen months after open reduction. Screw just removed. Index of motion, 83.



a b c

Fig. 7. Male, aged 15 years. a, Symptoms 2 weeks. Preslipping. Index of motion, 90. Pain and spasm. b, Three months after drilling and pegging. c, Five and one-half years after operation. Patient complains of no symptoms; he is fully active; index of motion, 100. This is an excellent result.

reduction, with early motion instead of plaster fixation would have given better results.

Open reduction. Eleven open reductions, 6 of them osteotomies through the proximal end of the neck, were reported in the first series. The operations were done some weeks after the slipping. The results were fair anatomically and functionally. We have done 17 open reductions from January, 1930 to 1939, all through the epiphyseal disc. These are divided into two groups. Eleven of the hips were immobilized in plaster for 10 to 12 weeks. Follow-up ranged from 2½ to 7 years, averaging 5½ years. There were only 2 good results, both having had preliminary rest with light traction, one being only 8 years old. The average index of motion was 26 (Fig. 2). Two were complete failures, one later having a fusion operation, the other an arthroplasty. In the second group of 6 hips, internal fixation was used, with active motion from the first week. The follow-up period averaged 2½ years. The ordinary nail, Smith-Petersen nail, and Lippman screw were each used in 2 cases (Figs. 3 to 6). The results in these 6 cases were far better, 2 being very good, 3 fair, and 1 poor. The average index of motion was 66, the range 36 to 96. There were altogether 5 good results and 9 fair ones among the 28 hips, leaving 14 or 50 per cent poor results. Slight arthritic lipping was usual in the hips followed several years. Internal fixation with early active motion is preferable when open reductions are done. When there is much limitation of motion and spasm, the operation should be preceded by a period of bed rest, preferably with suspension and light traction.

The drilling operation. We began to make the diagnosis of the preslipping stage some 10 years ago. It was thought that if the weight of the patient were kept off the hip, slipping would not occur and the lesion would heal. The first such patient was kept in bed several months until the line appeared healed. The epiphysis slipped as soon as she was allowed up. The next patient was allowed to go home to consider admission to the hospital. His epiphysis slipped suddenly on the way home. The preslipping hips have subsequently been treated as emergencies. It was obvious that if weight could be kept off the hip long enough, these lesions would heal. However, it seemed desirable to develop a surer and quicker method. The first operation for producing

a b c

Fig. 8. Male, aged 8 years. a, Slip ⅛ inch, symptoms 3 months. Index of motion, 87. Drilled July 31, 1931. No pegs. b, Six months after drilling; epiphyseal line healing. c, Eight months after drilling. A marked slip after a fall. Drilling without pegging does not produce rapid healing and union of the line.

premature union and healing of the epiphyseal line was done in December, 1930. The operation has been done upon 17 hips in the preslipping stage, and 23 with slight slips, to January, 1939. The Smith-Petersen approach was used. Several holes were drilled, curetted, or gouged from the neck across the epiphyseal disc into the head, and long thin fragments of bone from the ilium were inserted (Fig. 7). Every case has been carefully followed, the average period being 3½ years. The present report must be considered as preliminary, but the results to date have been very encouraging. There were no deaths or wound infections. There were 3 initial failures in the 40 cases; one preslip and 2 slight slips. One case, among the earliest, had no bone slivers inserted. No healing or union occurred and 6 months later the epiphysis slipped badly during a fall (Fig. 8) and an open reduction was done. In the second case, a boy of 11 years, the holes and slivers obviously did not cross the epiphyseal plate (Fig. 9). The lesion healed with rest but the epiphysis did not unite and 8 months later the condition recurred. A second successful drilling was then done. In the third case, a girl of 10 years, the lesion healed but the slivers absorbed and union did not occur. Eight months later the lesion recurred, and redrilling resulted favorably. Pegs were not used with two other drillings, and in these cases healing and union were quite slow. In the 35 remaining hips the lesion healed in 8 to 12 weeks and complete bony union across the epiphyseal plate occurred within 6 to 12 months without slipping. It may safely be said that if healing does not occur within these periods the pegs have not crossed the line. The patients were kept recumbent until the lesion healed and spasm subsided. Two of these patients had occasional pain during the follow-up period. Four had a slight residual limp, 4 did not attempt athletics because of obesity, and the remainder denied any symptoms whatever. There was shortening in only one-half of the cases, the greatest being one inch, the average one-sixth inch. Since little growth takes place at this epiphysis, the shortening is not enough to be of consequence. Internal rotation was slightly limited in 16 hips, flexion in 11, abduction in 9. Limitation of abduction appeared to be due in two of the latter hips to relative overgrowth of the greater trochanter. Arthritic lipping, however slight, was unusual in the longer follow-ups. The index of motion ranged from 66 to 100, and averaged 87. Thus the anatomic and functional results were very good or excellent in 39 of the 40 cases, including the two redrillings.

It is realized that these results might have been approximated by rest alone with freedom from weight bearing. This may be accomplished by rest in bed, or with a co-op-

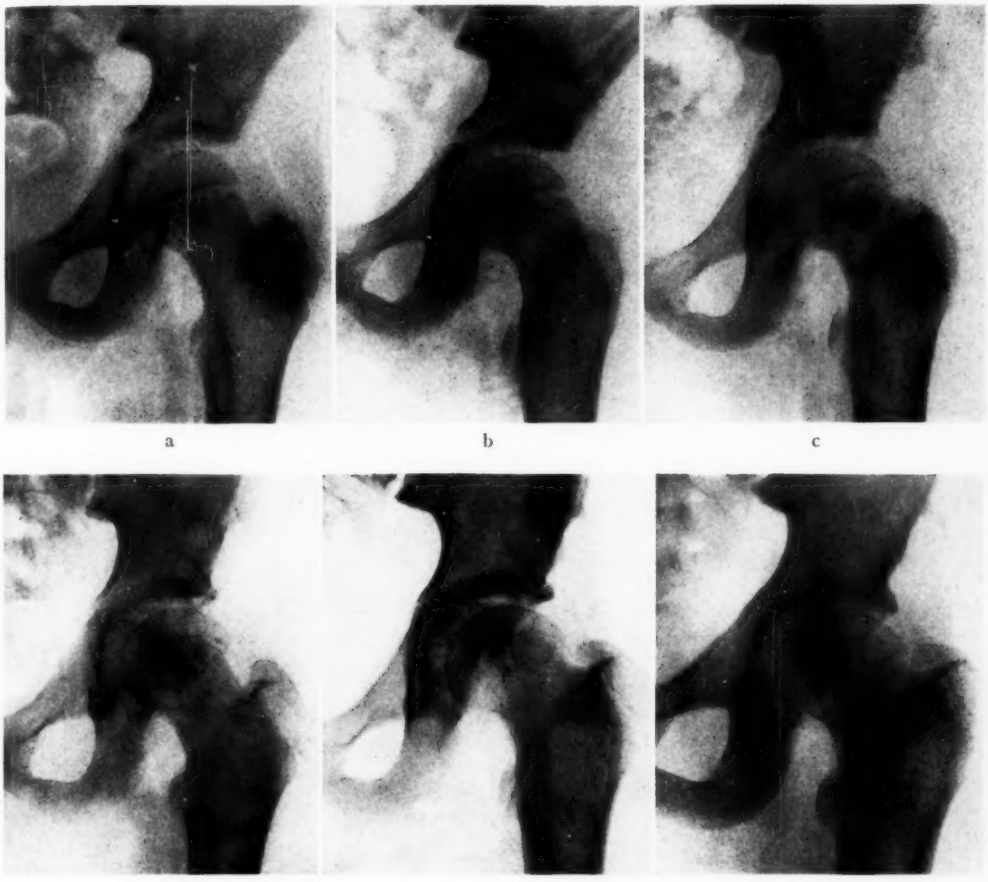


Fig. 9. Female, aged 11 years. a, Preslip. Symptoms 3 months. Index of motion, 52. b, Drilled and pegged January 27, 1937. Holes and pegs fail to enter head. c, Eight months after operation. Line not healed or united. Slight posterior slip. d, After second drilling and pegging. Holes and pegs enter head. e, Ten months after second operation. Line healed and united with no further slip. f, Roentgenogram which was taken 2 years after second operation. Line obliterated, head healthy. Index of motion 80.

erative, intelligent, and fortunate patient, by the use of crutches or a caliper brace. Such treatment would require months or even years in the younger patients. It is to the financial, psychological, physical, and temporal advantage of the patient and those who provide for his care that he be cured as quickly as is reasonably possible. We have not tried nailing these epiphyses because nailing, while it may prevent slipping, does not of itself produce union and it could hardly result in a quicker or more favorable healing. The drilling operation requires experience in hip surgery and gentleness, for a rough procedure will do more harm than good. The operation is advised under favorable circumstances as the simplest, quickest, and most certain method of curing the disease.

SUMMARY AND CONCLUSIONS

The clinical, laboratory, roentgenographic and pathological features of the preslipping

stage of slipping of the upper femoral epiphysis are described. These features are further discussed in relation to the slipping, quiescent, and residual stages.

The disease is found to be primarily a synovitis occurring during the period of rapid growth. The circulatory disturbance associated with the synovitis results in a softening on the distal side of the epiphyseal plate. The softening is often followed by a gradual or sudden and often progressive slipping of the epiphysis.

The results of the surgical treatment of 103 cases of this condition are reported. These are evaluated in terms of the normal hip and in relation to hips not surgically treated. The importance of rest in the treatment of the acute inflammatory phase of the preslipping or slipping stages is discussed.

Subtrochanteric osteotomy for correction of the deformity is preferred in the quiescent and residual stages.

Closed reduction by abduction and internal rotation has succeeded only in the few cases manipulated very soon after the first slip. Closed reduction by strong traction and by open operation have been usually anatomically successful. Limitation of motion with secondary circulatory changes in the united femoral head have been the rule in these three groups when the hips were immobilized in plaster after reduction.

Internal fixation with early active motion is preferred after closed or open reduction of the moderately or severely slipped epiphysis.

Hips seen in the preslipping stage or after a slight slip may be treated by rest and freedom from weight bearing but should not be immobilized in plaster. The possibility of recurrence of the lesion in younger children after roentgenographic healing of the disc must be emphasized. An operation for producing early healing and preventing any or further slipping is offered. The results in 40 cases having the operation have been excellent. The importance of early diagnosis and proper treatment before slipping occurs cannot be overestimated.

CHORIOEPITHELIOMA IN THE MALE

Treated with Pregnancy Serum

GRAY H. TWOMBLY, M.D., and ALFRED F. HOCKER, M.D.,
New York, New York

IN this paper we describe a case of chorioepithelioma of the testis treated by us at the Memorial Hospital, and show the results of various hormone tests made on the patient's urine and the effect on the gonadotropic hormone excretion levels produced by the injection of serum from parturient women and cord blood.

In a series of three review articles on the subject of chorioepithelioma in men and women, Mathieu makes repeated mention of the possibility that in the serum of the normal pregnant female there may be substances which are lytic for trophoblastic cells and cell emboli. Schmorl is credited with the observation that careful examination of the lungs of women dying during childbirth revealed that in 80 per cent of the number studied chorionic emboli were present. It has been reasoned that in many respects the growth of the placenta resembles that of a malignant tumor. It is true that chorionic villi invade the uterine musculature in a manner often suggestive of the behavior of a malignant tumor. Bell called attention to this invasive character of the placenta and was of the opinion that if the mechanism of nidation and placentation was thoroughly understood, much light would be thrown on the nature of cancer.

Since emboli from this invasive tissue break off and are carried to the lungs but fail to grow there or to produce metastatic tumors, several authors have suggested that there must be some substance present in the serum of pregnant women and animals which inhibits this growth. Dickson, referring to this possibility, suggests that the logical way to treat chorioepithelioma is by the injection of large quantities of serum from pregnant women or mares. Fortner and Owen believe that the treatment of chorioepithelioma may eventually be nonsurgical, consisting in serum injections or endocrine therapy. They say that "sera of pregnant animals are now being used but it is too early to expect accurate findings." They mention some work of Fraenkel who "demonstrated that the serum of normal pregnant women is lytic to chorionic epithelium while the serum of women with chorioepithelioma lacks this property." A study of Fraenkel's original paper fails to reveal any such researches. Furthermore, since the Fortner and Owen paper, there has been published, to our knowledge, no report on the progress of the treatment of chorioepithelioma with pregnant serum.

Since 1932, at the Memorial Hospital, 203 cases of tumor of the testicle have been studied by means of the quantitative Aschheim-Zondek test. Of this number 5 were classified by pathological examination as chorioepitheliomas. Of these 5 cases, all but one showed more than 10,000 mouse units per liter of the chorionic gonadotropic hormone. These patients were treated by intensive x-ray therapy in spite of which all quickly succumbed to the rapid progression of the tumor. Contrary to the opinion of some authors, we believe that this type of cancer is very resistant to radiation therapy. Therefore, since the patient, whose case report follows, revealed upon examination widespread metastatic disease, it was decided to follow the suggestions of Mathieu, Dickson, and Fortner and Owen, and give serum from pregnant women, studying carefully at the same time the effect of this treatment on the output of gonadotropic hormone in the urine as well as on the metastatic tumor nodules themselves.

A. L., a 33-year-old white male baker, born in Denmark, while driving his car along the road in January, 1940, noticed a tickling in his throat. On reaching home he examined this area with the aid

From the Memorial Hospital.

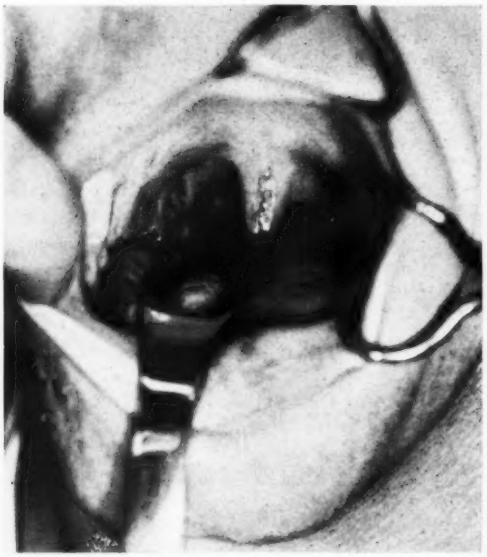


Fig. 1. Metastatic chorioepithelioma growing in the right tonsil; the area of tumor growth first discovered by the patient.

of a mirror and saw what he thought was a blood clot in the region of his right tonsil (Fig. 1). He tried to dislodge this material with a spoon but succeeded only in making the area bleed. A physician was consulted who advised tonsillectomy. This procedure was carried out but the specimen removed was discarded without further examination.

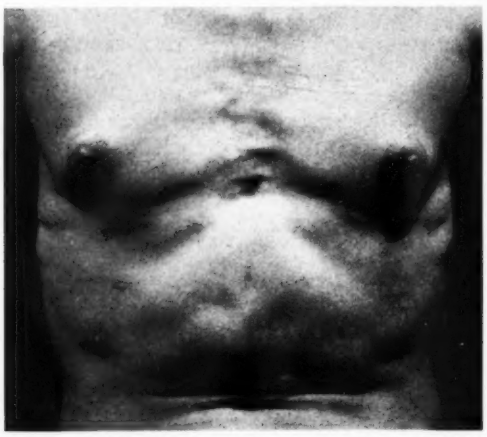


Fig. 3. Marked gynecomastia, accessory nipple beneath the right breast, and a metastasis to the left of the umbilicus.

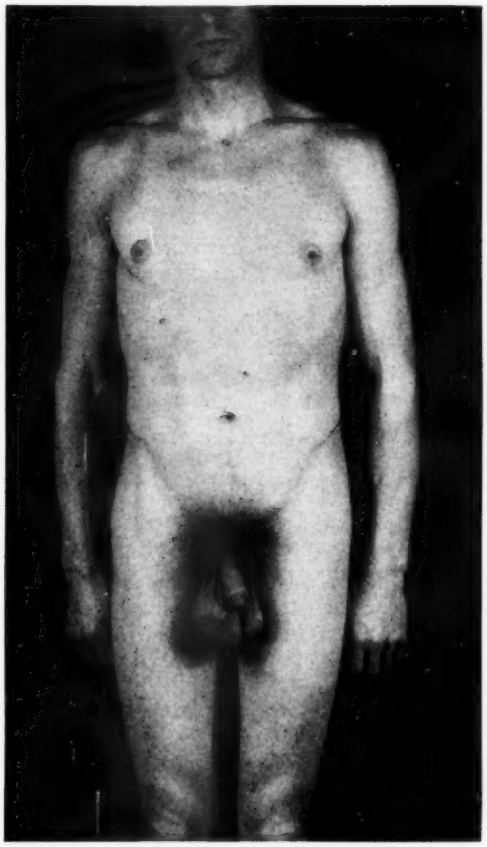


Fig. 2. Full length picture of patient showing testicular primary and metastases on chin and abdomen.

A week later a new-growth had appeared at the same site. This time another doctor was consulted who cauterized the area twice. Since 2 weeks later the tumor was still present and growing rapidly, this doctor referred the patient for diagnosis and treatment to one of us (A. H.).

The patient said he had always been well and strong. On close questioning, however, he admitted that for the past month he had felt a little tired and run down. He attached no special significance to this condition.

The complete examination of the patient showed in addition to the tumor of the tonsil, a similar nodule on the chin, a deep subcutaneous bluish nodule 1 centimeter in diameter in the left epigastrium, another nodule about the same size just above the iliac crest on the right, and a fifth one on the medial aspect of the right upper arm. The right testicle contained a hard tumor 6 by 7 by 7 centi-

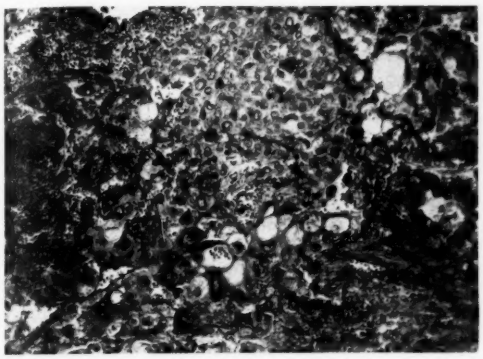


Fig. 4. Microscopic appearance of the tumor, showing syncytial and Langhans cells, hemorrhage, and hyalinizing necrosis.

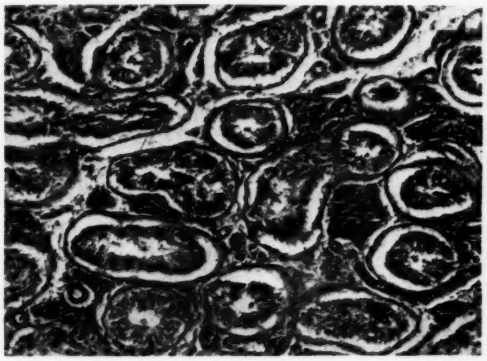


Fig. 5. Interstitial cell hyperplasia in the remaining testicular tissue, with complete failure in spermatogenesis.

meters (Fig. 2) which the patient thought had been present all his life. He had noticed, however, that it had grown slightly during the past 2 years. It had always been painless. He could remember no trauma to it. There was well marked bilateral gynecomastia (Fig. 3), a condition which the patient had first noted 2 weeks previously. Both breasts were slightly sore. The patient was very anemic. X-ray examination of the chest showed extensive bilateral metastases.

In addition to the physical findings already mentioned, a blowing systolic murmur was heard over all the precordium but loudest in the second interspace to the left of the sternum. The blood pressure was 140/60. The liver and spleen were not palpable. The genitalia were not remarkable save for the tumor of the right testicle. The prostate was small. The seminal vesicles seemed somewhat enlarged.

The laboratory findings were: urine, clear; specific gravity, 1020; no albumin or sugar; sediment negative. Blood tests showed hemoglobin, 30 per cent; red blood cells, 2,396,000; white cells, 8,600; polymorphonuclears, 83 per cent; monocytes, 2 per cent; lymphocytes, 15 per cent. There was marked variation in the size and shape of the red cells. The results of the special hormone determinations will be given later.

The patient entered the Hospital on February 2, 1940. He was given transfusions on February 5, 9, 12, and March 1 with 500 cubic centimeters of citrated whole blood on each occasion. From February 5, 1940, to February 26, 1940, he received daily small amounts of deep x-ray therapy. These were directed as follows: upper torso, 25r 8 times to a 50 by 50 centimeter field; lower torso, 25r 8 times to a 50 by 50 centimeter field. The factors were 200 kilovolts; target-skin distance, 150 centimeters; 0.5 millimeter copper filtration. The vertex of the skull was given one treatment of 200r to a 14 by 12 centimeter field, 250 kilovolts, 50 centimeter target-skin distance, 1.5 millimeters copper filtration.

The lesion of the tonsil was treated through a 3 centimeter per oral cone at a target distance of 38 centimeters with 400r, 500r, and 500r at weekly intervals. It did not regress.

The lesion on the chin was implanted with one gold filtered radon seed of 1.82 millicuries. It continued to grow.

The patient rapidly declined and he died on March 9, 1940.

Autopsy findings. In addition to the subcutaneous, pharyngeal, and testicular tumors already mentioned, the postmortem examination revealed metastatic deposits in the pleura, lungs, mediastinum, liver, spleen, kidneys and para-aortic nodes, and brain. These were friable and hemorrhagic in appearance. There were several hundred of them in the lungs varying in size from a few millimeters to 3½ centimeters. Most of the metastases in the liver were near the surface in the right lobe. The largest was 2 centimeters in diameter. There were 3 nodules in the spleen, the largest 1.5 centimeters in diameter. Multiple cortical metastases of small size were present in the kidneys. Two nodules were present along the iliac arteries and four similar metastases along the aorta measured 2 to 2.5 centimeters in diameter. In the right occipital lobe of the brain was a 1 centimeter metastatic area, with several smaller metastases deep in the cerebrum. Two metastatic tumors occurred in the cerebellum, the larger 2 centimeters in diameter.

The testicular tumor measured 7½ centimeters in greatest diameter. It was composed largely of typical chorioepithelioma most of which was infarcted, necrotic, and interspersed with extensive areas of hemorrhage (Fig. 4). Parts of the tumor showed cysts lined with columnar mucus secreting epithelium or with stratified squamous epithelium. These structures would seem to indicate the origin of the chorioepithelioma in a complex teratoma of the testis. The remainder of the atrophied testicular tissue formed a narrow rim around the tumor. In

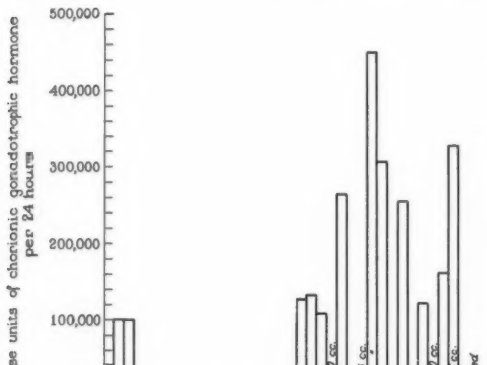


Fig. 6. Chart of the urinary excretion rate of chorionic gonadotropic hormone before and after treatment with serum from parturient women and cord blood.

this area there was well marked interstitial cell hyperplasia (Fig. 5).

A bilateral confluent lobar pneumonia involved all lobes. There were several red, friable, easily detached vegetations on the pulmonary and mitral valves. An incidental finding was a double ureter on the right side.

The pituitary was unusually interesting. It has been reported by Heidrich, Fels and Mathias that histological changes similar to those seen in the pituitary gland of pregnancy occur in the glands of men dying of chorioepithelioma. Stoeckl reported, contrary to this observation, that there was a great increase in deeply granular basophiles. In the present case the pituitary was sectioned and examined by Dr. Aura E. Severinghaus, who reported as follows:

"The anterior lobe of the hypophysis showed features which are characteristic of the pituitary gland of the pregnant female at full term. The acidophiles were markedly degranulated, and many cell-cords were entirely composed of these cells, which are the so-called pregnancy cells. The basophiles were numerous and well granulated. Cytological features which have been associated with increased secretory activity in the cell were prominent in both granular types."

On biological test, the dried gland when ground up and suspended in normal saline failed to cause any changes in the ovaries of immature female rats 21 days old even when given in amounts corresponding to 7 milligrams of dry gland. Normal males, according to Witschi and Riley, have glands which produce vaginal cornification, and ovarian follicular ripening in doses of 1 milligram of dried gland. This decrease in pituitary potency corresponds with the findings in the glands of pregnant women.

Special hormone determinations and treatment—gonadotropic hormone. On admission the patient's entire urinary output was collected for 3 days and the number of mouse units of chorionic gonadotropic hormone was determined for each 24 hour output. Before any treatment of any sort had been given these assays showed 40,000; 100,000; and 100,000 mouse units, respectively.

A similar 3 day run was made on February 21, 22, and 23. At this time in spite of 12 treatments with deep roentgen therapy, the total amounts were essentially the same, 125,000; 130,000; and 115,000.

On February 24 the patient was given 250 cubic centimeters of serum intravenously, the serum having been obtained from the blood of two mothers who were in the fourth postpartum day. The result of this procedure, shown in the chart (Fig. 6), was characterized by a sharp rise in the gonadotropic hormone to 260,000 mouse units per 24 hours.

On February 27 there was given intravenously 125 cubic centimeters of sterile serum obtained from numerous specimens of placental blood, taken from the cord at the time of delivery. This procedure was followed by a temperature rise to 103 degrees but since the patient did not appear particularly sick another 125 cubic centimeters of serum was given the following day, February 28. The urine specimen collected from 8:00 a.m. February 28 to 8:00 a.m. February 29 showed the highest output of gonadotropic hormone recorded for this patient, 440,000 mouse units. The next day, February 29, in spite of continuing high fever the output had dropped to 300,000 mouse units. Two days later, March 2, a day following a transfusion of 500 cubic centimeters of normal citrated blood, the temperature rose to 104.4 degrees F, while the gonadotropic output fell to 250,000 mouse units. Physical signs at this time suggested bilateral bronchopneumonia. Sulfapyridine was given resulting in a prompt fall in the patient's temperature to 99.2–100.8 degrees. The urinary output of gonadotropic hormone on March 4 was 120,000 mouse units. In brief, then, the injections of 250 cubic centimeters of post-partum serum and placental blood serum appear to have raised the urinary gonadotropic hormone excretion from 130,000 mouse units to a maximum of 440,000 mouse units from which point the excretion rate slowly sank to the pre-treatment level. These variations seemed to occur independent of the patient's temperature changes. A similar rise did not follow transfusion with normal male blood.

Two more injections of serum from women 1 to 3 days postpartum were given, the first of 250 cubic centimeters on March 5, and the second of 175 cubic centimeters on March 7. Urinary excretion

of gonadotropic hormone on March 6 had risen to 160,000 mouse units, and on March 7 it was 320,000 mouse units. As the patient's condition became rapidly worse this was the last determination made. He died on March 9 at 7:00 p.m.

From this report we see that there was not only an initial rise in excretion rate after the first sera injections with a return to normal 5 days after their discontinuance, but a second rise following two subsequent injections.

Estrogenic hormones. Urine collected for 3 days, February 2 to 5, on the patient's admission, before he had received any therapy was assayed by a modification of the method of Smith and Smith (19) for the three estrogenic hormones, estrone, estriol, and estradiol. The figures obtained from this 72 hour specimen are 53.3 gamma of estrone, 10.7 mouse units[1] of estradiol, and 80 mouse units of estriol. From February 21 to 24 another 72 hour specimen was similarly analyzed and found to contain 111 gamma of estrone, 90 mouse units of estradiol, and 60 mouse units of estriol.

These figures are higher than we have found in the urine of any other male or menopausal female patient we have tested, and they are comparable only with the figures found in the midcycle in menstruating women.

Androgens. The same specimens used for the determination of estrogenic excretion rate were also used, after separation into phenolic and neutral fractions, for the determination of the androgens. The colorimetric method of Callow was followed. In the first 72 hour specimen 72 milligrams of "Androsterone equivalent" were found, that is, the color given with the Zimmerman reagent, dinitrobenzene, was equivalent to that produced by 72 milligrams of androsterone. This amount is roughly 24 milligrams a day, a not unusual figure for a normal man. This colorimetric test is specific only for those neutral steroids having a ketonic group in the 17 position and tells nothing about the biological activity of the material.

Consequently we assayed the neutral fraction on the comb growth that could be produced in day-old white leghorn pullets (Dorfman). By this method the neutral fraction was found to contain the equivalent of 3.1 milligrams of androsterone per 24 hours, in its comb stimulating ability. From our experience this is within the range of normal, though perhaps a little lower than the average.

On the second 72 hour specimen collected from February 21 to 24 only the colorimetric type of assay was done. It showed a total "androsterone equivalent" of 17 ketosteroids of 58.8 milligrams or 19.6 milligrams per 24 hours.

[1]Mouse unit=amount necessary to cause full estrus in ½ of 8 spayed mice injected with the material twice a day for 2 days. The smears were read at 72 hours after the first injection.

Pregnandiol. Since in many ways this man's condition was analogous to pregnancy in the female, two assays were made of the product, pregnandiol, shown by Venning and Browne (23) to be the form in which progesterone is excreted in the urine. The amounts of pregnandiol found in the urine during pregnancy are considerable. Bachman, Leekley and Hirschmann report 10 milligrams at the twelfth week of pregnancy to 110 milligrams a week before the onset of labor.

In our patient two 48 hour collections of urine were made, one from February 5 to 7 and the other from February 16 to 18. In each of these an attempt was made to extract sodium pregnandiol glucuronidate by the method of Venning and Browne (22). The material so extracted was rather gummy and did not crystallize well at first. It was redissolved repeatedly in alcohol and recrystallized on a steam bath. Finally after washing with petroleum ether, 16.5 milligrams of a clear crystalline substance was obtained from the first specimen and 10.5 milligrams from the second.

Some of these crystals were sent to Dr. Browne who reported that Dr. Venning found them to melt at 210 degrees with the evolution of gas. He said: "the material contains less than 1% of glucuronic acid; it is therefore not a glucuronide. It gave only 1 degree depression of the melting point of pure pregnandiol, so it could probably be free pregnandiol."

If this material was in fact pregnandiol, it would be a finding of considerable interest since such material has not been found in the urine of normal men. It had been thought at one time that pregnandiol was formed only by the action of endometrium on progesterone but this idea has been disproved by the work of Buxton and Westphal who showed that progesterone injected into normal men or men with Addison's disease, may be excreted as pregnandiol. Hamblen, Cuyler and Hirst have confirmed this and have shown, also, that desoxycorticosterone acetate, an adrenal hormone, may also be secreted in this form. Hirschmann found pregnandiol in the urine of ovariectomized women, and Marker found it in the urine of bulls, but not in that of steers. Obviously the precursor of the compound, if progesterone, in these cases, does not come from the corpus luteum, and the logical conclusion is that it is of adrenal origin since it has been established that progesterone is capable of replacing the adrenal cortical hormones in adrenalectomized animals. (Thorn, Engel and Eisenberg, 21; Gaunt, Nelson and Loomis, 9.)

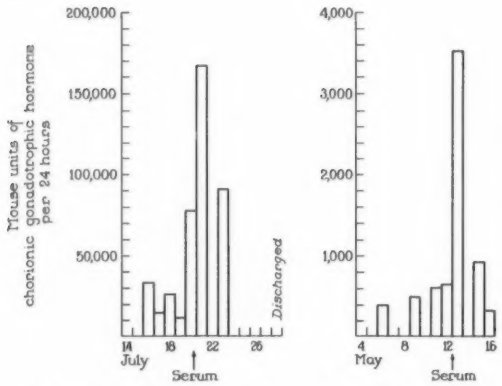


Fig. 7. Chart of the urinary excretion of chorionic gonadotropic hormone in two patients treated with goat serum having a high "antihormone" titre. The goats had been injected over a prolonged period with extracts of pregnancy urine.

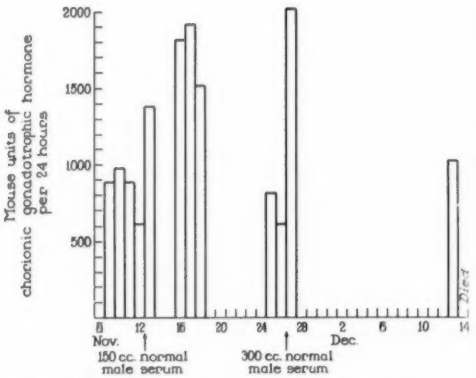


Fig. 8. Chart of the urinary excretion rate of chorionic gonadotropic hormone by a patient receiving injections of normal male serum.

RÉSUMÉ

Our greatest interest in this case was to discover whether the treatment with the serum of pregnancy would have any effect on the course of the disease or the hormone levels. Obviously such an effect would open possibilities in the treatment of these hopeless types of patients. Previous papers had set forth the logic for such an approach but had given no data. Our expectation was that if any antisubstances were present, these would tend to depress rather than elevate the excretion levels of gonadotropic hormone. The unexpected rise which this form of therapy brought about can be explained in several ways. It may come from the excretion of the hormone contained in the injected serum, through the patient's urine, though this seems hardly likely. Smith and Smith (18) give values of 25 to 200 rat units of gonadotropic hormone present per 100 cubic centimeters of serum at the end of pregnancy. A rat unit is usually said to equal 5 mouse units of chorionic gonadotropic hormone, but allowing for all possible errors it is inconceivable that the administered serum could have contained more than 2 to 4 thousand mouse units while the observed increase in the urine was 300,000 mouse units.

The second possibility is that some specific antisubstance is present in the pregnancy serum which either stimulates the tumor cells to greater excretion, damages them with a resulting agonal release of hormone, or changes the kidney threshold for hormone excretion. That there may be some specific effect of this kind is also suggested by 2 other cases (Fig. 7). Both of these were treated by anti-sera made by injecting goats with pregnancy urine extract until there were present large quantities of antipregnancy "anti hormone." The sera were supplied through the kindness of Dr. A. S. Parkes. In the first case, the serum was rather toxic, giving redness, soreness, and edema at the site of injection. The second serum was not locally toxic. Both gave tremendous rises in the rate of gonadotropic hormone excretion. In neither case was the patient noticeably benefited; both died ultimately of uncontrolled testicular cancer.

The third and most likely explanation for the rise in excretion rate of gonadotropic hormone is that it was brought about by some nonspecific protein shock-like reaction following the injection of foreign protein. The pregnant serum was not typed. The cord serum showed very slight amounts of hemolysis, and the patient showed a rise in temperature the day following the serum injection though this was later ascribed to bronchopneumonia.

To test this hypothesis further another patient with teratoma testis has been studied recently in the Hospital (Fig. 8). This man had an excretion rate of 880, 960, 880, and 600

mouse units on 4 succeeding days after admission. He was then given 150 cubic centimeters of normal male serum, following which his output rose to 1,360, 1,800, and 1,900. Fourteen days later 300 cubic centimeters of normal male serum was given and his output rose from 800 to 2,000. It sank again to 1,000 the day before his death. The fact that untyped normal male sera intravenously gave a similar though less pronounced effect on gonadotropic hormone excretion in the urine of this patient suggests that nonspecific serum therapy rather than the presence of an antigonadotropic substance caused the changes in gonadotropic hormone excretion rate in the patient with chorioepithelioma.

The normal androgenic excretion rate and the high estrogenic hormone found in the urine explain the gynecomastia, since development of the breast can be brought about in the male by the injection of estrogenic substances. Where the estrogenic hormones come from, whether they arise from the tumor itself or from the adrenals, and what rôle the hypertrophied interstitial cells of the testes play is still unknown. The presence of pregnandiol in the urine suggests abnormally stimulated adrenals though the morphology post mortem was not abnormal. Perhaps the estrogenic hormone also came from the adrenals.

SUMMARY

1. Chorioepithelioma of the testis in a man of 33 with autopsy findings is described.

2. The pituitary gland showed both an increase in basophilic cells and the degranulation of the eosinophils characteristic of pregnancy. Biologically, no gonadotropic potency could be demonstrated in the acetone dried gland.

3. The patient excreted in his urine from 40,000 to 130,000 mouse units of chorionic gonadotropic hormone daily. This amount was increased up to 440,000 mouse units by the injection of 250 cubic centimeters of serum from the blood of parturient women and 250 cubic centimeters of serum from cord blood. This increase may have been due to some specific antisubstance in such sera rather than to added chorionic gonadotropic hormone or protein shock. The likelihood is that it was due to nonspecific protein shock.

4. The patient excreted in one 72 hour specimen 533 mouse units of estrone; 10.7 mouse units of estradiol, and 80 mouse units of estriol. In another specimen were 1,110 mouse units of estrone, 90 mouse units of estradiol, and 60 mouse units of estriol. These quantities, which are higher than any found in this laboratory for normal men or menopausal women and comparable, but higher than in normal menstruating women, appear to explain the patient's marked gynecomastia.

5. The androgenic hormone output was normal by colorimetric and biological test.

6. Extraction of two 48 hour specimens of the patient's urine showed 16.5 milligrams and 10.5 milligrams, respectively, of a crystallized hormone thought to be pregnandiol.

REFERENCES

1. Bachman, Carl, Leekley, Dorothy, and Hirschman, H. J. Clin. Invest., 1940, 19: 801–807.
2. Bell, W. Blair. J. Obst. & Gynæc., Brit. Emp., 1928, 35: 233.
3. Buxton, C. L., and Westphal, U. Proc. Soc. Exper. Biol. & Med., 1939, 41: 284–287.
4. Callow, N. H., Callow, R. K., and Emmens, C. W. Bio-Chem. J., 1938, 32: 1312–1331.
5. Dickson, J. C. U. S. Navy M. Bull., 1935, 33: 358–362.
6. Dorfman, R. I., and Grenlich, W. W. Yale J. Biol. & Med., 1937, 10: 79–88.
7. Fortner, H. C., and Owen, S. E. Am. J. Cancer, 1935, 25: 89–97.
8. Fraenkel, E. Samml. klin. Vortr., n. F., 1897, No. 180.
9. Gaunt, R., Nelson, W. O., and Loomis, E. Proc. Soc. Exper. Biol. & Med., 1938, 39: 317.
10. Hamblen, E. C., Cuyler, J. K., and Hirst, D. V. Endocrinology, 1940, 27: 172–179.
11. Heidrich, L., Fels, E., and Mathias, E. Beitr. z. klin. Chir., 1930, 150: 347–384.
12. Hirschmann, H. J. Biol. Chem., 1940, 136: 483–502.
13. Marker, R. E. J. Am. Chem. Soc., 1938, 60: 2931–2933.
14. Mathieu, A. Internat. Abstr. Surg., 1939, 68: 52–70.
15. Ibid, 181–198.
16. Mathieu, A., and Robertson, T. D. Internat. Abstr. Surg., 1939, 69: 158–175.
17. Schmorl, G. Quoted by Dunger, R. Page 339. Beitr. z. path. Anat., 1905, 37: 279–375.
18. Smith, O. W., and Smith, G. van S. Am. J. Obst. & Gynec., 1937, 33: 365.
19. Smith, O. W., Smith, G. van S., and Schiller, S. Endocrinology, 1939, 25: 509–519.
20. Stoeckl, E. Zentralbl. f. Gynaek., 1933, 57: 2614–2618.
21. Thorn, G. W., and Engel, L. L. J. Exper. Med., 1938, 68: 299–312.
22. Venning, E. H. J. Biol. Chem., 1937, 119: 473–480.
23. Venning, E. M., and Browne, J. S. L. Soc. Exper. Biol. & Med., 1936, 34: 792–793.
24. Witschi, Emil, and Riley, G. M. Endocrinology, 1940, 26: 565–577.

CARCINOMA OF THE GALL BLADDER AND EXTRAHEPATIC BILE DUCTS

A Clinical and Pathological Study of 117 Cases in 13,330 Necropsies

JACK D. KIRSHBAUM, M.S., M.D., and DONALD D. KOZOLL, M.D.,
Chicago, Illinois

ALTHOUGH a moderate literature exists concerning carcinoma of the gall bladder and, to a less extent, carcinoma of the extrahepatic bile ducts, a considerable proportion of this material consists of operating room specimens. Clinical correlations with large series of post-mortem examinations are few enough in number to have permitted erroneous conceptions concerning the relative frequency of lesions producing the syndrome of malignant obstructive jaundice, the progression of symptoms, the tendency for metastasis, and the manner of exitus.

In a series of 13,330 consecutive post-mortem examinations performed in the Department of Pathology of the Cook County Hospital between January, 1929, and April, 1940, inclusive, we collected 55 cases of primary carcinoma of the gall bladder and 62 cases of primary carcinoma of the extrahepatic bile ducts. The first 12 cases of our series of carcinomas of the extrahepatic bile ducts were included in a report from this laboratory by Shapiro and Lifvendahl in 1931. Certain conclusions drawn by these authors bear revision in the light of a more extensive series. One case of melanoblastoma of the gall bladder was previously reported from this laboratory by Rosenthal in 1931.

INCIDENCE

Of the 13,330 autopsies 1,808, approximately 13.6 per cent, revealed malignant tumors. (For statistical purposes we have included sarcomas and malignant neurogenic tumors with carcinomas.) Fifty-five cases of carcinoma of the gall bladder constitute 0.41 per cent of all post-mortem examinations and 3.0 per cent of all carcinomas. This compares favorably with the incidence of 0.27 per cent of 11,400 post-mortem examinations reported by Jankelson, and 0.33 per cent of 13,034 autopsies reported by Illingworth. In a recent rather complete statistical review of the literature on carcinoma of the gall bladder Mohardt quotes an incidence of 0.85 per cent among 19,908 necropsies reported by von Berencsy and von Wolff. Among the various authors quoted by Mohardt in establishing the frequency of involvement by cancer of the gall bladder compared to other organs, the values varied from 3 to 13 per cent. In our series the average was 3.0 per cent.

The surgical incidence of carcinoma of the gall bladder is considerably higher than the autopsy incidence and probably less reliable. In a series of papers from the Mayo Clinic the incidence of malignancy decreased from an original report in 1902 of 5 per cent of all diseased gall bladders to a recent figure of 0.5 per cent. Mohardt found an average of 1.12 per cent gall bladders to be malignant in a composite review of over 35,000 operations.

Sixty-two cases of carcinoma of the extrahepatic bile ducts constitute an incidence of 0.46 per cent of all post-mortem examinations and 3.4 per cent of all carcinomas. They were located as follows: in the cystic duct, 7 cases; hepatic ducts, 13 cases; common bile duct, 32 cases; papilla of Vater, 10 cases. Rolleston's 90 cases of carcinoma of the extrahepatic bile ducts were located as follows: in the cystic duct, 6 cases; common hepatic duct, 19 cases; common bile duct, 34 cases; juncture of cystic, hepatic, and common bile ducts, 27 cases; right and left hepatic ducts, 3 cases;

From the Division of Surgery, Northwestern University Medical School, and Department of Pathology, Cook County Hospital, and Woodlawn Hospital.

cystic and common bile ducts, 1 case. Carcinoma of the papilla of Vater is conspicuously absent in this series. In Marshall's series the juncture of the cystic, hepatic, and common bile ducts was the most frequent site; next, the papilla of Vater; and third, the hepatic duct. In McLaughlin's collective review, the common bile duct was the most frequent site whereas the point of confluence of all three ducts was second in frequency; Pallin's statistics are similar with the exception of a higher incidence of involvement of the papilla of Vater. Inasmuch as the point of confluence of the cystic, common hepatic, and common bile ducts is within such close proximity to carcinomas originating in any one of the converging ducts, this area might easily be the most frequent site of secondary extension. In our experience we have been able to localize the tumor to one of the ducts in almost every case.

AGE AND SEX

Of the 55 cases of carcinoma of the gall bladder, 21 occurred in males and 34 in females. Of the 55 cases 44 were in the white race and 11 in the negro. Before comparison of our figures for sex and racial incidence can be accurately made with that in the literature, the following fact must be taken into account: that about twice as many autopsies are performed in this institution upon males as upon females, and about twice as many in the white race as in the negro. Therefore, the absolute figures will be as follows: 76.4 per cent of carcinomas of the gall bladder occurred in the female and 23.6 per cent in the male; 66 per cent were of the white race and 34 per cent in the negro. The youngest patient with carcinoma of the gall bladder was 42 years old, and the oldest was 86 years old. The distribution of cases among the age decades was as follows: in the group from 41 to 50 years, 7 cases; 51 to 60 years, 18 cases; 61 to 70 years, 20 cases; 71 to 80 years, 7 cases; 81 to 90 years, 3 cases.

This distribution of cases according to age compares very favorably with a similar classification of 212 cases of carcinoma of the gall bladder recorded by Judd and Gray. The average age varies in different series from 57 to 60 years. Mohardt cites several cases reported in the literature of carcinoma of the gall bladder in patients 22 and 25 years of age. Mohardt has gathered the results of 9 different contributors who gave figures of from 54 to 100 per cent of all carcinomas of the gall bladder occurring in the female. Perhaps the explanation for this wide range lies in the failure to recognize a disproportion in the incidence of post-mortem examinations between the two sexes. Our corrected figure of 76 per cent appears to coincide with the average.

Forty-four of the 62 cases of carcinoma of the extrahepatic bile ducts occurred in the male and 18 in the female. Of these patients 54 were white, 7 were negroes, and 1 was oriental. The absolute figures for the sex and racial incidence of carcinoma of the extrahepatic bile ducts were 55 per cent in the male and 45 per cent in the female. There were 77.1 per cent in the white race, 20.1 per cent in the negro, and 2.8 per cent in the yellow. Judd and Gray found 58 of 100 cases in the male and in Rolleston's series of 90 cases of bile duct cancer, 55 were in the male. Devic and Gallavardin observed the incidence in their series to be 30 in the male and 16 in the female. Musser's cases were equally divided. The youngest patient was 31 and the oldest 86 years old. The distribution among the age decades was as follows: in the group from 31 to 40 years, 5 cases; 41 to 50 years, 9 cases; 51 to 60 years, 15 cases; 61 to 70 years, 21 cases; 71 to 80 years, 11 cases; 81 to 90 years, 1 case.

The marked predilection of carcinoma of the gall bladder for the female, in sharp contrast to carcinoma of the gastrointestinal tract in general, has been widely appreciated and attributed to the preponderate incidence of cholelithiasis in the female. Although we found that carcinoma of the extrahepatic bile ducts showed a definite tendency to occur at an earlier age than carcinoma of the gall bladder, yet the occurrence of the majority of the cases was in the sixth and seventh decades. This is in complete agreement with other investigators.

CLINICAL PICTURE IN CARCINOMA OF THE GALL BLADDER

In no clinical entity is a closer relationship between symptomatology and pathology more

Fig. 1. (P.M. 478–40) Clinically silent carcinoma of the papilla of Vater. Note metastases to the regional lymph nodes and liver. Patient died of peritonitis following a recurrent perforation of a posterior duodenal ulcer.

evident than in carcinoma of the biliary structures. For this reason we find it difficult to group the symptoms found into definite symptom-complexes such as has been done by Lancereaux and by Rolleston. We prefer to report our findings upon a statistical basis, bearing in mind all the while that each clinical history is entirely dependent upon the sequence of pathological events within the porta hepatis, based upon pre-existing pathological changes as well as upon those in the making.

In 34 of our 55 cases, 61.8 per cent, there were complaints of pain at some time during the clinical course; pain was most frequently referred to the right upper quadrant, less frequently to the epigastrium, and least frequently to the right lower quadrant. The severity of pain was seldom such that demanded morphine for relief; it was usually described as a chronic recurrent type of dull pain. In 16 of the series a definite history suggestive of previous gall-bladder disease could be established. Five patients who complained of pain during the clinical course were found at autopsy not to have either cholecystitis or cholelithiasis. On the other hand, there were 13 cases of cholelithiasis, with or without cholecystitis, in which the patient did not experience pain. It has been our experience at the Cook County Hospital that although 9 per cent of all post-mortem examinations reveal gall stones, 88 per cent of the cases were without symptoms. Therefore, we must include some other factor in addition to cholelithiasis for the explanation of pain in carcinoma of the gall bladder. With an incidence of pain in over 60 per cent, we cannot agree with Upcutt who lists as the most striking clinical features of cancer of the gall bladder, the absence of pain, intense jaundice, and extreme emaciation.

Jaundice occurred at some time in the clinical course of 34, or 61.8 per cent of the 55 patients. In the majority of cases it was present at the time of admission, was persistent and progressive, and associated with clay-colored stools in 12 cases. Of the 34 cases 14 were associated with pain and 11 without pain; on the other hand, 20 cases of the series of 55 in which pain was a factor were not associated with jaundice. Seven patients of the 55 developed jaundice as a terminal condition and are therefore not included among the 34 with symptomatic jaundice. The icterus index

levels were constantly elevated in all cases of jaundice, ranging from 65 to 250, but usually less than 100. The van den Bergh test, when made, gave a direct immediate reaction.

Gastrointestinal symptoms were listed in 30 of the 55 patients and usually consisted of a vague dyspepsia, anorexia, nausea, and occasional vomiting. Although these symptoms frequently led to the suspicion of carcinoma of the stomach, their relative mildness together with the usual presence of the characteristic pain, with or without jaundice, militated against such a diagnosis. Diarrhea, constipation, and melena were rather infrequent complaints. Judd and Baumgartner divided the cases of gall-bladder carcinoma as follows: a group comprising 70 per cent of the cases which presented history of biliary colic and dyspepsia dating back many years and then a sudden appearance of jaundice, dull pain, and a palpable tumor; a second group of 22 per cent listed complaints compatible with chronic cholecystitis alone; the remaining 8 per cent presented themselves in a terminal state with evidences of cachexia, carcinomatosis, jaundice, and ascites. On account of the nature of our institution, a much larger proportion of our patients constitutes this latter group.

Thirty-one of the 55 cases were admitted in a state of cachexia; this might be anticipated in a large municipal charity institution. Weight loss was sometimes extreme, as much as 60 pounds in 6 months but usually in the vicinity of 20 pounds during the course of the illness. In 12 of these 31 cases the patient complained of a palpable mass. The duration of illness was usually between 3 and 6 months, the shortest being 1 month and the longest 3 years; only 9 of the 55 patients lived more than 6 months after the initial complaint. Judd and Gray found that in most of their 212 cases of carcinoma of the gall bladder, the duration of illness was less than 6 months, and that in one-half of these symptoms had persisted for 2 months or less. Twenty-two of the 55 patients presented complaints of dependent edema and ascites, the ascites frequently requiring abdominal paracentesis.

On physical examination, 35, or 63.3 per cent, of 55 patients presented a palpable liver; 13 presented a palpable gall bladder, and 4 others presented a palpable extrahepatic mass. In only 2 instances was the gall bladder alone palpable. The presence of a palpable gall bladder in only 23.6 per cent of these cases places considerable doubt on the value of this finding, despite its frequent emphasis by earlier writers. Twenty-one, or 38 per cent, of these cases proved to have a fluid wave suggestive of ascites.

In 20, or 36.3 per cent, a profound secondary anemia was found, 7 cases showed blood in the stool, and in another 7 cases no free acid was shown on gastric analyses. The gall bladder failed to concentrate x-ray opaque dyes in 10 instances and x-ray opaque stones were visualized in 2 cases. The nonprotein nitrogen and creatinine were frequently elevated depending upon the intensity of the jaundice, but an albuminuria was very common. Cholesterol levels of the blood were determined in only 4 patients, but in all of these it was much higher than normal. It became apparent that laboratory aids in the diagnosis of carcinoma of the gall bladder are of only slight help. However, our series of cases show a greater tendency for secondary anemia than is ordinarily believed to be present in this neoplasm.

CLINICALLY SILENT CARCINOMA OF THE GALL BLADDER

We wish to draw special attention to 4 cases of carcinoma of the gall bladder which we believe were clinically "silent." At least they presented no symptoms or physical findings which could warrant a diagnosis, and we mention them to illustrate the insidious nature of the disease. A 60 year old colored female was believed to have peritonitis, of which she died a few days after admission; however, the cause of the peritonitis was found at autopsy to be due to a spontaneous ulceration of the gall bladder into the colon, the fundus of the gall bladder containing a polypoid adenocarcinoma without evidence of metastasis. Another 60 year old colored female died of peritonitis due to a traumatic rupture of the rectum, but in addition a scirrhous adenocarcinoma of the fundus of the gall bladder was found which had extended

into the liver bed. A 48 year old colored male was believed to have a central nervous system syphilis, but on post-mortem examination these symptoms proved to be due to a melanoblastoma of the neck of the gall bladder which had metastasized to the brain, as well as elsewhere. A 59 year old white female presented the classical symptoms and signs of pernicious anemia with cord degeneration, of which she died. At autopsy she presented a papillary adenocarcinoma of the gall bladder which had metastasized to the liver and produced a spontaneous cholecystoduodenostomy.

CARCINOMA OF THE EXTRAHEPATIC BILE DUCTS

Pain was present in 26, or 41.9 per cent, of 62 cases. The pain was usually of dull character, most frequently localized in the mid-epigastrium and less frequently to either right quadrant of the abdomen. Fourteen of the 26 patients complaining of pain were without evidence of cholecystitis or cholelithiasis; on the other hand, 6 cases of cholelithiasis and 2 of cholecystitis did not list pain as a symptom. Eleven of the 62 patients gave a definite history of previous gall-bladder colic. The fact that a source other than the gall bladder must be looked for as the explanation of pain becomes even more apparent in carcinoma of the extrahepatic bile ducts than in carcinoma of the gall bladder. Musser has demonstrated the invasion of the nerve bundles of hepatic ducts by the neoplastic cells and offers that for the explanation of pain. Of a series of 20 patients with carcinoma of the bile ducts reported by Renshaw 12 experienced pain varying from a dull ache to severe biliary colic; 11 of his patients gave a history of cholecystitis or cholelithiasis for an average length of time of 5 years.

Of the 62 patients with bile duct cancer 57, or approximately 92 per cent, presented jaundice as a dominant symptom sometime during the clinical course, the majority of these patients noting this complaint early in course of the illness. Jaundice is still recognized as the most reliable symptom, for above all other symptoms it focuses attention directly upon the porta hepatis. The 5 remaining cases which did not list jaundice as a symptom constitute a group of cases to which we shall refer to shortly as clinically "silent" lesions of the extrahepatic bile ducts. In 26 of the 57 jaundiced patients, pain of a type described was also present. The jaundice was associated with acholic stools in 29 instances and with the complaint of biliuria in 5. Pruritis is a frequent accompaniment. The jaundice is almost invariably unremittent once established, but early in the clinical course the jaundice may be transient. This type is supposedly due to temporary edema or spasm of the common duct which is spontaneously relieved. Shapiro and Lifvendahl mention the ulceration of an obstructing neoplasm of the common duct as the mechanism of temporary resumption of bile flow late in the disease. We have seen 3 cases of carcinoma in the vicinity of the ampulla of Vater which have become necrotic and ulcerated into the duodenum; however, in none of these was there relief from the obstruction to bile flow. Therefore, we cannot see any value in utilizing this as a differential point between carcinoma of the papilla of Vater and carcinoma of the head of the pancreas.

Here, as in carcinoma of the gall bladder, the frequency of mild complaints referable to the gastrointestinal tract, is surprisingly high. In 32 of the 62 patients there was nausea, anorexia, and vague dyspepsia. Constipation was more common than diarrhea. Complaints of postprandial pain relieved by soda or food was not altogether uncommon. Five patients of the series of bile duct cancer were found to have chronic duodenal ulcers and in 1 instance a severe duodenitis. This is of particular interest in that the malignant transformation of a duodenal ulcer has been suggested as a possible pathogenetic agent in carcinoma of the common bile duct and papilla of Vater, just as is gastric carcinoma.

Of the 62 patients with bile duct carcinoma 34 patients showed evidences of cachexia and weight loss, frequently extreme. Four patients complained of palpable masses on admission. The average duration of the illness is definitely shorter than for carcinoma of the gall bladder. We found that in most cases it varied between 2 and 4 months, only 1 pa-

tient surviving after 1 year. Probably this fact is to be explained by an earlier cholemia rather than a more malignant neoplasm.

In 30 of the 62 cases dependent edema and ascites suggested portal obstruction in the differential diagnosis.

In view of former teaching, tabulation of physical findings is rather disappointing. In 37 of the 62 cases the liver was palpable and in only 19 was the gall bladder palpable; this gives a percentage of palpable gall bladders on clinical examination of approximately 30 per cent. In a series of 20 cases of bile duct cancer reported by Renshaw, only 6 had palpable gall bladders. Courvoisier's law is verified to a much greater extent by laparotomy and autopsy than by bedside examination. Other palpable metastatic extrahepatic masses were noted in 4 cases.

A profound secondary anemia was observed in 19 of the 62 cases. A markedly elevated icterus index was characteristic, frequently in the neighborhood of 100 units; repeated determinations showed a tendency to rise rather than decrease just prior to death. Biliuria was consistent and usually marked. Chemical blood was observed in the stools of 35 of the 62 patients, an observation that has received little emphasis. Melena is no more characteristic of carcinoma of one area of the extrahepatic biliary system than of another. Gastric analyses revealed an achlorhydria in 8 of 62 cases. In 13 of the patients there was a failure of the gall bladder to visualize and in 2 gall stones were seen. In 4 the nonprotein nitrogen rose slightly above 40 milligrams per cent, but in all other cases it was within normal range as was the creatinine. Albuminuria appears to be a frequent accompaniment of icterus. Blood cholesterol was determined in only 5 cases and showed marked elevations in all instances. While van den Bergh tests were not made routinely, when performed they showed a direct immediate reaction.

That the diagnosis of primary carcinoma of the gall bladder or extrahepatic bile ducts is difficult is not to be disputed. The most difficult concept to alter is that carcinoma of the head of the pancreas is the most frequent cause of progressive jaundice which is associated with a distended gall bladder and generalized cachexia. It has been our experience that both carcinoma of the extrahepatic bile ducts and carcinoma of the gall bladder occur more frequently than carcinoma of the head of the pancreas (41 cases) as a cause of obstruction of the biliary tract. Moreover, we have found pain to be associated with the jaundice in all 3 of these malignancies far more often than heretofore acknowledged. Clinical diagnosis in 55 cases of carcinoma of the gall bladder included: primary carcinoma of the gall bladder, 12 cases; carcinoma of the extrahepatic bile ducts, 3 cases; carcinoma of the head of the pancreas, 2 cases; carcinoma of the gastrointestinal tract, 16 cases; carcinoma of the liver, 5 cases; cholecystitis and cholelithiasis, 4 cases; peritonitis, 1 case; carcinoma without known primary site, 2 cases; miscellaneous (including "silent" cases) 6 cases; no diagnosis, 4 cases.

The diagnosis was correct in 21.8 per cent of the cases. The clinical diagnosis in 62 cases of carcinoma of the extrahepatic bile ducts included: carcinoma of the head of the pancreas, 20 cases; carcinoma of the gastrointestinal tract, 12 cases; carcinoma of the extrahepatic bile ducts, 13 cases; carcinoma of the gall bladder, 3 cases; portal cirrhosis, 4 cases; primary carcinoma of the liver, 2 cases; cholecystitis and cholelithiasis, 3 cases; obstructive jaundice (cause unknown), 3 cases; peritonitis, 1 case; perforated peptic ulcer, 1 case. The diagnosis was correct in 20.9 per cent of the cases.

Rolleston states that in not one of 48 cases of carcinoma of the gall bladder reported from Guy's Hospital was a correct diagnosis made. Similarly, Boyce and McFetridge report only 2 cases in 25 in which a correct diagnosis was made before operation and 4 cases of carcinoma of the gall bladder in which it was suspected. Only 2 cases in Jankelson's series of 48 gall-bladder carcinomas were diagnosed correctly. In view of the fact that the 3 cardinal findings, viz., pain, jaundice, and a palpable tumor, are not always associated in one case, diagnostic errors appear quite understandable.

We would like to describe in some detail those cases to which we have already alluded

as "silent" carcinomas of the extrahepatic bile ducts. The popular concept of a neoplasm of the biliary tract is that occlusion occurs early in its course and subsequently is followed by icterus. In 5 cases the neoplasm was an incidental finding at necropsy and was not directly contributory to the cause of death.

CLINICALLY SILENT CARCINOMA OF THE EXTRAHEPATIC BILE DUCTS

CASE 1. A colored male of 67 years entered the hospital with symptoms of dull epigastric pain, nausea, anorexia, vomiting, ascites, and dependent edema; within 1 week the patient died of an acute fibrinous peritonitis, and at autopsy an infiltrating adenocarcinoma of the cystic duct with metastases was found. The gall bladder was shrunken and the liver of normal size.

CASE 2. A white female 76 years of age presented symptoms suggesting carcinoma of the stomach and organic heart disease; the patient died of bronchopneumonia after a month's stay in the hospital, and the post-mortem examination revealed an infiltrating adenocarcinoma of the common bile duct which had extended to the liver and pancreas without producing obstruction of the duct itself.

CASE 3. A white male 61 years of age entered the hospital with a history suggestive of alcoholic cirrhosis of the liver; the patient died following a massive hematemesis. At necropsy a ruptured esophageal varix associated with an atrophic cirrhosis of the liver in addition to a papillary adenocarcinoma of the common bile duct was found notwithstanding the fact that there was a congenital absence of the gall bladder and cystic duct.

CASE 4. A white female 40 years of age died of peritonitis following subtotal gastrectomy for recurrent perforation of a posterior duodenal ulcer; at autopsy a medullary adenocarcinoma of the papilla of Vater with metastases to the peribiliary, peripancreatic, and periesophageal lymph nodes was found (Fig. 1).

CASE 5. A colored male 31 years of age entered the hospital with symptoms of intestinal obstruction which abated with conservative treatment. It was later thought that a tuberculous peritonitis was present and on autopsy an infiltrating adenocarcinoma of the cystic duct with generalized metastases was found which had not encroached upon any of the other biliary structures.

PATHOLOGY

Carcinoma of the gall bladder and carcinoma of the extrahepatic bile ducts have essentially the same pathological types and our description shall apply to both. We have included 2 cases of sarcoma along with these to facilitate discussion, for other than its histological differences it deserves no separate mention. We have classified the various histological types in Table I.

TABLE I.—CLASSIFICATION OF HISTOLOGICAL TYPES OF CARCINOMAS STUDIED

	No. cases	Total
Gall bladder		
Infiltrating adenocarcinoma	27	
Papillary adenocarcinoma	14	
Mucus-producing adenocarcinoma	3	
Medullary carcinoma	8	
Sarcoma	2	
Melanoblastoma	1	
Total cases of carcinoma of gall bladder	55	55
Extrahepatic bile ducts		
Cystic duct		
Infiltrating adenocarcinoma	6	
Medullary carcinoma	1	7
Common hepatic duct		
Infiltrating adenocarcinoma	10	
Papillary adenocarcinoma	3	13
Common bile duct		
Infiltrating adenocarcinoma	24	
Papillary adenocarcinoma	5	
Medullary carcinoma	3	32
Papilla of Vater		
Papillary adenocarcinoma	7	
Infiltrating adenocarcinoma	2	
Squamous cell carcinoma	1	10
Total cases of carcinoma of extrahepatic ducts		62

Papillary adenocarcinoma is thought to originate from benign papillomas of the mucosa either of the gall bladder or the duct involved; the relative frequency with which benign papillomas of the gall bladder are encountered in surgically removed gall bladders is 10 per cent according to Judd and Baumgartner. The papillary adenocarcinoma is a fungating mass which projects into the lumen; in the bile ducts it is frequently pedunculated. On histological examination, the tumor cells cover a central stalk of connective tissue. This type of carcinoma may replace the gall bladder from within and is apt to produce an empyema of the gall bladder by direct extension of the polypoid tumor into the cystic duct; however, we have seen empyemas of the gall bladder associated as frequently with infiltrating and scirrhous adenocarcinomas as with papillary adenocarcinoma. The latter does tend to undergo more rapid necrosis and therefore pre-

disposes to infection of the gall bladder. This type of tumor is less invasive and less malignant and should permit a longer life span although our records of the duration of illness show no significant difference to justify this conclusion; similarly, our statistics on the frequency of metastasis show no lessening of that tendency in this type of tumor.

The infiltrating adenocarcinoma appears to be by far the most frequent type of tumor encountered. It is composed of atypical alveoli of tumor cells which invade all the layers of the gall bladder or biliary duct and convert it into a rather rigid, contracted organ. In the biliary tract this type of tumor takes the appearance of an ulcerated thickened plaque overlying and replacing the mucous membrane. This tumor is prone to produce a shrunken gall bladder or a stenotic duct. As the histological term of this tumor suggests, it tends to invade adjacent structures early and produce widespread metastases. It is considered far more malignant than the papillary adenocarcinoma. The degree of fibrous tissue reaction varies.

Next to the stomach, the gall bladder is supposed to be the most frequent site for the production of mucus-producing carcinomas. It is a degenerative change expressive of an overactivity of the mucus-producing activity of the glands of the gall-bladder mucosa. This is the type of tumor most apt to cause a spontaneous perforation of the gall bladder into a neighboring viscus; however, none of our examples of this complication occurred in this type of carcinoma. Perforation of the gall bladder was seen as frequently with papillary as with infiltrating or scirrhous adenocarcinomas. All 3 cases of mucus-producing adenocarcinoma occurred in the gall bladder and none was found among the biliary tract neoplasms. All 3 cases showed metastases. Although this type of tumor occasionally gives rise to a Krukenberg tumor of the ovary, none of our patients developed metastasis to the ovary.

Although medullary carcinoma is better used as a term of gross description, we imply a tumor that has a solid grayish-white appearance not unlike the white matter of the cerebral cortex which on histological examination is composed entirely of closely packed alveoli filled with tumor cells with little intervening stroma. Of 6 such cases, 3 occurred in the gall bladder and 3 in the extrahepatic bile ducts. The tumor is quite malignant and shows widespread metastasis.

Squamous cell carcinoma most likely originates from metaplastic mucosal epithelium which is probably a response to chronic inflammatory change. This at least is comparable to the formation of squamous cell carcinomas in other organs normally lined by cylindrical epithelium. Clinical reports of squamous cell carcinoma of the gall bladder exist in fair number, but few of these are described in the bile ducts. Our only case of this type involved the papilla of Vater, the tumor ulcerating into the duodenum and metastasizing to the regional lymph nodes and the liver. The clinical picture in this case was a classical one of malignant biliary obstruction. Fehr and Cabot have reported similar cases.

Although sarcoma of the gall bladder is reputedly rare, we have 2 cases in our series of 55, previously reported by Ragins. Neither of these 2 tumors produced jaundice, and the patient died of the metastasis rather than of the usual cholemia. Rolleston gathered 19 cases of sarcoma of the gall bladder from the literature. The most recent case report is that of Erdmann.

Among the more rare tumors we found in the gall bladder was a melanoblastoma in a 37 year old colored male to which we have already referred. A primary melanoma of the ampulla of Vater is described by Duval.

The obstruction to bile flow can be accomplished by one of three mechanisms or a combination of them: (1) annular stricture of the rigid carcinomatous duct; (2) plugging of the lumen by a projecting polypoid mass; and (3) pressure of enlarged metastatic peribiliary lymph nodes. According to Vander Veer and to Wahl, the low pressure of the bile and spasm of the smooth muscle structures within the biliary tract are additional factors favoring obstruction. To this might be added inflammatory changes due to stones, and edema of the mucosa which are frequently found to be associated with the neoplasm.

The fate of the liver in carcinoma of the gall bladder or bile ducts may result in: (1) an obstructive biliary cirrhosis; (2) an ascending cholangitis; (3) liver abscess; and (4) massive metastases. In biliary cirrhosis the liver is usually enlarged, exceedingly firm, has a dark green hue, and on section the marked dilatation of the extrahepatic bile ducts is prominent. The histological picture is one of marked imbibition of bile pigment by the parenchyma, bile casts in the dilated biliary capillaries, and a marked proliferation of fibrous tissue and lymphocytes within the portal triads. Occasionally a zonal necrosis of the liver lobule is noted. Cholangitis tends to produce a much softer liver which on section will leave pus on the cut surface. On histological examination the thickening of the portal triads is found to be due not only to increased fibrous tissue but to an acute inflammatory exudate which consists of polymorphonuclear leucocytes and pus cells which tend to surround the proliferating distended bile ducts. Although the sinusoids contain large numbers of leucocytes the liver parenchyma is uninvaded unless the cholangitis has progressed to the point of abscess formation. The liver abscesses usually tend to be small; they are scattered everywhere throughout the parenchyma and are filled with a light green, purulent material. The abscesses produce local necrosis with compression atrophy of the adjoining parenchyma.

A central zone of necrosis of the liver lobule due to the stasis of bile and a resultant reversal in direction of the flow of bile occur, according to Fueterrer. Herring and Simpson produced a similar result in experimental obstruction of the bile duct.

In carcinoma of the gall bladder, evidence of an obstructive biliary cirrhosis was seen in 26 cases; it is frequently difficult to tell how much of the liver enlargement is due to the cirrhosis and how much to the metastases, for the liver was the site of metastasis in 35 of 55 cases. Obstructive cirrhosis is more common in carcinoma of the extrahepatic bile ducts. We found biliary cirrhosis in 51 of 62 cases of bile duct cancer; although the liver was the site of metastasis in an identical number, it does not necessarily imply that the two processes were always coexistent.

There were 7 instances of cholangitis in the cases of carcinoma of the gall bladder and 3 in carcinoma of the extrahepatic bile ducts; the difference can be correlated with the greater frequency of empyema of the gall bladder in cases of carcinoma of the gall bladder. There were 3 cases of liver abscess in 55 cases of gall-bladder carcinoma and 2 cases of liver abscess in the 62 cases of bile duct carcinoma.

Of 55 cases of carcinoma of the gall bladder, 20, or 36.3 per cent, gave evidence of cholecystitis and 40, or 72.6 per cent, gave evidence of cholelithiasis. In 8 of the 40 cases, stones were found in the bile ducts as well. In the series of cases from 24 different authors cited by Mohardt, the incidence of calculous carcinomatous gall bladders varied from a low of 64.6 per cent to a high of 100 per cent. In our own series of 13,300 consecutive autopsies, the post-mortem incidence of gallstones was 9 per cent, 88 per cent of these being without clinical history referable to the gall bladder. The incidence of calculous gall bladders which develop carcinoma is 3 per cent in our series. Among 17 contributors listed by Mohardt, this figure ran from 1.14 to 15 per cent, the average being 4 to 5 per cent. It has been our experience that 6 per cent of all men past 50 and 14 per cent of all women past 50 possess gall stones at autopsy.

Of 62 cases of carcinoma of the extrahepatic bile ducts, 14, or 22.5 per cent, gave evidence of cholecystitis and 19, or 30.6 per cent, gave evidence of cholelithiasis. Three of the 19 cases contained stones within the common duct. Gallstones were present in about one-third of the cases of Rolleston's series of bile duct carcinomas. In each of McGlinn's 5 cases of bile duct cancer, out of 9,000 post-mortem examinations gallstones were present. The incidence of common duct stones is usually placed at 15 per cent of all cases of cholelithiasis. Mayo-Robson considers gallstones a greater factor in the etiology of cancer of the bile ducts than is generally accepted.

Of our 41 cases of carcinoma of the head of the pancreas 8, 14.5 per cent, showed cholecystitis and 4, 9 per cent, cholelithiasis.

Most authors have accepted the rôle of cholelithiasis in the etiology of carcinoma of

the gall bladder as certain. The reasons for this have been chiefly two: First is the frequent association of carcinoma of the gall bladder and stones, of which our figures are quite representative. That stones should cause cancer has been explained by the possibility that the chronic irritation they induce might predispose to cancer, that the stones possessed some radioactive substance (Lazarus-Barlow), and finally that the stones might contain some carcinogenic agent. The second piece of evidence is the experimental production of cancer of the gall bladder in guinea pigs by the introduction of gall stones and foreign bodies. This work had long been accepted and confirmed until investigators, such as Burrows, pointed out that though a stone might produce a cystic hyperplasia of the mucosa of the gall bladder, this was a far cry from cancer itself.

The fact that the disease normally has an incidence of only 14 per cent gall stones in the sex and age group which it most frequently attacks, together with the fact that in a closely related disease—carcinoma of the extrahepatic bile ducts—the incidence of stones is 30.6 per cent, which few will accept as the etiological factor in that disease, should deter us somewhat from overemphasizing cholelithiasis as the sole possible etiological agent. Ewing suggests a combination of multiple factors including the irritative effect of calculi, cellular hyperplasia following inflammation, high cholesterol concentration within the gall bladder, and the irritative effect of bile.

To complete the discussion on the etiology of neoplasm as far as the extrahepatic bile ducts themselves are concerned, some interesting suggestions first made by Rolleston should be mentioned. He suggested the malignant transformation of an ulcer of the biliary tract mucosa, such as occurs in a small percentage of peptic ulcers, as the mechanism in the origin of bile duct cancers. Two case reports by MacCarty emphasize this possibility. Both of these duodenal ulcers involved the papilla of Vater and produced a clinical picture of obstructive gall-bladder disease rather than peptic ulcer.

We have already stated that Courvoisier's law is verified more often by post-mortem studies than by clinical experiences. In the 55 cases of carcinoma of the gall bladder, the gall bladder was found to be distended in 16 cases, and in the group of carcinomas of extrahepatic bile ducts, distention of the bile ducts was noted 18 times. Doubtless dilatation of the gall bladder occurs most frequently when the neck of the gall bladder is involved, and dilatation of the bile ducts is probably a compensatory action rather than an obstructive phenomena. In 10 cases the gall bladder was markedly shrunken and only 1 of them was infected. The shrunken gall bladders were always seen associated with infiltrating or scirrhous carcinomas. Hydrops of the gall bladder was seen in 5 cases, in 2 of these the clear mucinous fluid filled a gall bladder of normal size. Eleven cases of empyema of the gall bladder were found, 6 associated with marked distention of the gall bladder. In all but 2 of the 11 cases of empyema, stones were present, and in all 5 cases of hydrops stones were present.

In carcinoma of the extrahepatic bile ducts the gall bladder was distended in 39, or 62.9 per cent, and there was a distention of the bile ducts above the site of obstruction in 48, or 77.2 per cent, of the cases. Musser lists dilatation of the ducts in 9 of his 18 cases of cancer of that structure, whereas Devic and Gallavardin described 7 distended gall bladders in 14 cases of cancer of the cystic, hepatic, and common bile ducts. Courvoisier stated that dilatation of the gall bladder occurs in 84 per cent of all cases of cancer involving the bile ducts. It has been our experience and that of others that this figure is too high and that actually it lies between 50 and 60 per cent. There were 6 instances of hydrops of the gall bladder, in only 3 were stones present, and in 2 the gall bladder was not significantly enlarged. There were 4 cases of empyema of the gall bladder in this series and all of them were associated with stones and distention of the gall bladder.

Other complications of carcinoma of the biliary tract not already mentioned include perforation, pericholecystic abscess, and biliary peritonitis. In 55 cases of carcinoma of the gall bladder there were 3 perforations into the peritoneal cavity, 5 into the colon, and 3 into the duodenum. In 3 of these 11 cases, per-

foration was followed by a fatal biliary peritonitis. Spontaneous perforation of a carcinomatous gall bladder occurred in 10 of Musser's 100 cases and in 6 of Reidel's 77 cases. Boyce reports 2 cases of perforation into the peritoneal cavity in 25 cases of carcinoma of the gall bladder. Four cases of pericholecystic abscess were seen, and usually the extension was directly into the liver bed. There was 1 case of liver abscess and 1 subphrenic abscess, both of which ruptured into the peritoneal cavity and led to a fatal purulent peritonitis. Biliary peritonitis followed cholecystostomy in 1 instance whereas 1 case of biliary peritonitis was seen to develop without any apparent mechanical leak.

In 62 cases of carcinoma of the extrahepatic bile ducts there were 4 cases of biliary peritonitis, all without evidences of a mechanical leak; these were attributed to a transudation of gall bladder contents through its distended edematous wall. Three other cases of biliary peritonitis followed surgical procedures. One case of fibrinous peritonitis followed subtotal gastrectomy for a perforating ulcer, and another case was apparently hematogenous in origin. In 1 case a large pericholecystic abscess ruptured and produced a purulent peritonitis.

Ascites was a frequent finding. This is attributed to the following: carcinomatosis of the peritoneum and mesentery, obstruction to the portal vein by pressure of metastatic lymph nodes or intrahepatic tumor masses, and cirrhosis of the liver.

The effect of the carcinoma of the biliary tract upon the pancreas is not often mentioned. Although experimental mechanical occlusion of the pancreatic duct is supposed to produce an acute necrosis of the pancreas, no instance of this was found in our entire series, although the pancreatic duct was often occluded to the extent of producing a marked dilatation of the duct of Wirsung. This occurred in 3 cases of gall bladder carcinoma and 11 cases of extrahepatic bile duct carcinoma. The changes found in the pancreas were as follows: In carcinoma of the gall bladder, 2 cases showed an atrophic fibrosis of the pancreas, 2 showed some fat necrosis, and 1 showed an extensive lipomatosis; while in carcinoma of the biliary tract, there were 10 cases of an atrophic fibrosis, and in 5 some degree of fat necrosis. Disturbed pancreatic function was not observed.

Another frequently overlooked factor in the syndrome of obstructive jaundice is the effect of the cholemia on the kidneys. Changes occur in the renal tubules such as deposits of bile in the tubular epithelium and formation of bile casts. This condition is known as "icteric nephrosis" (a form of tubular nephrosis). Albuminuria and nitrogenous retention are frequently observed clinically. Among the gall-bladder carcinomas 17 cases and among the bile duct carcinomas 24 gave definite evidence at autopsy of an icteric nephrosis. At necropsy these kidneys are swollen, deeply icteric, and have a very soft consistency.

Although metastasis of carcinoma of the gall bladder is generally accredited with being widespread and occurring early, the same concept is not applied to carcinoma of the extrahepatic bile ducts. In Marshall's series of bile duct cancers, about 25 per cent of his cases showed metastases. Renshaw stated that metastasis of cancers of the extrahepatic bile ducts "seldom occurs." He quotes the statistics of Devic and Gallavardin that metastatic growths were present in only 20 per cent of their cases. Musser lists 10 instances of metastasis in 18 such cases. Renshaw believed that distant metastases were rare and suggested that on laparotomy, "small nodules in the liver produced by peripheral dilatation of the small intrahepatic ducts may be mistaken for metastases." In our experience, 76.7 per cent of our cases of carcinoma of the extrahepatic bile ducts showed definite evidences of metastases and listing of the sites for metastases showed a diversity second only to carcinoma of the gall bladder.

The frequency with which certain sites are involved by metastases can be better appreciated by a short review of the lymphatic supply of the gall bladder and bile ducts. A plexus of lymphatics lies beneath both the mucosa and serosa of the gall bladder with short communicating vessels between them. The main lymphatic vessels drain to a sentinel lymph node usually located at the cystic duct. This lymph node receives similar afferent

lymphatics from the common bile duct, duodenum, and pancreas. Efferent lymphatic vessels extend from this lymph node up along the biliary tract and portal vein into the hilus of the liver. Therefore, a carcinoma of the gall bladder would tend to metastasize to the liver both by direct extension and by lymphatic spread. Bile duct carcinoma, on the other hand, extends first by way of the lymphatics, which in turn may involve adjacent organs. However, because of the close proximity of the hepatic ducts to the liver parenchyma, early direct extension may take place from that site. The lymph nodes involved are the cystic nodes, the peribiliary, peripancreatic, and periaortic nodes. The carcinoma may then spread to the mediastinal nodes, then to the tracheobronchial nodes, and finally to the supraclavicular lymph nodes. In that manner we frequently see a Virchow's node as in carcinoma of abdominal organs other than the stomach. Hematogenous dissemination undoubtedly occurs but is relatively infrequent. Distant metastases are much more common in our series than is usually reported. Table II shows the frequency with which the various sites were involved.

The 14 cases of carcinoma of the extrahepatic bile ducts without metastases were distributed as follows: 7 were located within the common bile duct, 5 involved the papilla of Vater, and 2 the common hepatic duct.

Analysis of the metastatic characteristics of the 2 neoplasms shows that the gall-bladder carcinomas tend to metastasize more frequently and to involve more structures. Undoubtedly this is largely due to its contiguity with the liver. Such distant metastases as the brain, heart, thyroid gland, and lung are indicative of a hematogenous spread. Although the right lower pulmonary lobe is supposed to be the most frequent site for pulmonary metastasis by way of the retrodiaphragmatic lymph nodes, enough other pulmonary lobes were involved to explain a hematogenous route. Although cases of Addison's disease have been reported by Warthin as due to the metastases of gall-bladder carcinoma, we have failed to find any in our material.

Among unusual symptoms produced by the metastases which complicated the diagnosis we may list the case of a 37 year old colored woman who had an ulcerating lesion of the left breast which was treated as a scirrhous carcinoma. The area was treated with the x-ray prior to biopsy. The biopsy specimen suggested a metastatic hepatocellular carcinoma. The necropsy 1 year later revealed a medullary carcinoma of the common bile duct with metastases to the liver and skin of the left breast. One case of melanoblastoma of the gall bladder produced brain metastasis; the symptoms produced were attributed to central nervous system lues. None of our gall-bladder carcinomas metastasized to the ovary, which would label it a Krukenberg tumor. Such a case was reported by Shelley and Ross. Although Cooper, in his recent review of carcinoma of the papilla of Vater, quoted 20 per cent as the incidence of metastasis for that structure, we have found it to be 50 per cent.

The most common cause of exitus in these cases was found to be cholemia which is

TABLE II.—FREQUENCY AND SITE OF METASTASIS

Site of metastasis	55 cases of carcinoma of gall bladder No. cases	62 cases of carcinoma of extrahepatic bile ducts No. cases
No metastasis	2	14
Liver	51	35
Lymph nodes	34	28
Peritoneum	7	9
Omentum	10	4
Mesentery	8	4
Extrahepatic bile ducts	10	3
Gall bladder	0	4
Pancreas	3	10
Duodenum	3	4
Jejunum	1	0
Pylorus (stomach)	1	2
Colon	6	0
Lungs	9	6
Adrenal	5	5
Kidney	3	1
Pleura	1	3
Rectum	2	2
Spleen	2	1
Diaphragm	1	1
Pouch of Douglas	3	0
Urinary bladder	1	0
Heart	1	0
Thyroid	1	0
Portal vein	1	0
Uterus	1	0
Umbilicus	1	0
Brain	1	0
Seminal vesicle	0	1
Skin of breast	0	1
Pancreatic duct	0	1
Ureter	0	2

associated with cachexia and carcinomatosis in the majority of cases. Death is usually precipitated by an intercurrent bronchopneumonia. The less frequent causes of death occurred in the following order of importance: carcinomatosis and cachexia without cholemia, peritonitis due to various causes already described, bronchopneumonia, postoperative shock, and spontaneous hemorrhage.

TREATMENT

Nothing more than disappointing results can be expected in the treatment of a disease inherently so difficult to diagnose as carcinoma of the gall bladder, especially in an early stage when treatment might be of some avail. To be sure the picture here presented is a gloomy one, for it is only the patients with unsatisfactory results who come to autopsy. We hope, however, that in revealing these frustrated attempts at surgical cure something may be gained from previous errors and a new method of procedure evolved.

Prophylactic removal of a diseased gall bladder affords faint hope in the treatment of carcinoma of that organ. In the hands of most surgeons the operative mortality following operations for cholelithiasis is less than that following operations for the removal of a carcinomatous gall bladder. Hence the possibility of the presence of a carcinoma of the gall bladder has been accepted by most surgeons as an indication for cholecystectomy. Erdmann's is the only dissenting voice in this popular opinion, for in his experience contrary to that of all others, the operative mortality following operation for cholelithiasis was twice as great as that for carcinoma. Judd and Baumgartner attributed the decreased incidence of carcinoma in surgical gall bladders of from 5 per cent to less than 0.5 per cent at the Mayo clinic to the earlier removal of diseased gall bladders.

Duodenal drainage together with repeated serum bilirubin determinations are of use in deciding upon the urgency for surgery. If no bile is recovered on repeated duodenal aspirations and the serum bilirubin remains high or mounts, obstruction is complete and there is every disadvantage in delaying operation. But, if occlusion of the biliary tract is only partial as shown by recovery of bile on aspiration and there is a decline in the serum bilirubin, some time may be devoted to preoperative therapy such as the administration of fluids, proteins, and vitamins. With the newer methods of controlling the hemorrhagic tendencies associated with icterus, surgical mortality should be materially reduced. Pallin in 1921, attributed one-half of 25 immediate postoperative deaths in 31 operative cases of carcinoma of the bile ducts to postoperative hemorrhage. The same author has stated that the danger from cholemia is not great until icterus has persisted for from 3½ to 4 weeks and therefore that surgery should be attempted within 3 weeks of the onset of unremittent jaundice. The use of duodenal aspiration to differentiate carcinoma from cholelithiasis, and carcinoma of the ducts from carcinoma of the head of the pancreas, is fraught with considerable inaccuracy. An impacted stone may produce the same clinical picture as a neoplasm, and we have seen a carcinoma of the head of the pancreas occlude the common bile duct by metastasis long before it had produced obstruction of its own duct.

Not only is the clinical diagnosis difficult but accurate location of the primary lesion even at the time of laparotomy is fraught with considerable difficulty, especially when the lesions involve the lowermost portions of the common bile duct and the papilla of Vater. We have found 5 instances in our series in which laparotomies performed by capable surgeons revealed what was thought to be carcinoma of the head of the pancreas but at post-mortem examination was proved to be a carcinoma of the extrahepatic bile ducts. The error, we believe, lies in the popular misconception of the relative frequency of these two lesions and in the fact that a normal pancreas frequently feels exceedingly hard. We have already stated that in our series of cases, we have found that carcinoma of the head of the pancreas is a poor third as the etiological agent of malignant obstruction of the biliary tract. Moreover, experience at the necropsy table reveals that an apparently normal pancreatic gland is frequently hard in consistency. The picture is further complicated by the

tendency for fibrotic changes to occur within the pancreas in cases of obstructive jaundice.

In 3 of our 55 cases of carcinoma of the gall bladder cholecystectomy had been carried out at least 6 months prior to the onset of the present illness. Cholecystostomy was carried out in 2 cases and jejunostomy in 1, as palliative procedures. Nature was kind to 8 of the 55 cases in which a spontaneous cholecystocolostomy or cholecystoduodenostomy occurred, but the success of this procedure was short-lived in 3 of these cases, for the patients died soon after of biliary peritonitis.

Cholecystostomy was performed in 5 of the 62 patients with bile duct carcinoma, cholecystogastrostomy for another 4 patients, and cholecystoduodenostomy for still another. One of these patients had in addition to a carcinoma of the common bile duct an independent primary carcinoma of the pylorus of the stomach; the latter neoplasm was the one recognized at laparotomy, and the widespread metastases which were found at that time were believed to be due to it but later proved to be due to the carcinoma of the bile duct. Radical resection of the involved parts was not attempted in any of our cases. It is, indeed, a formidable procedure from which recovery is a singular feat. The palliative procedure of biliary enteric anastomosis overcomes the complication of cholemia, gall-bladder infection, and cholangitis, and decreases the spasm of the duct by eliminating the back pressure of a distended gall bladder.

SUMMARY

From a series of 13,300 consecutive autopsies, of which 1,808 were primary malignant neoplasms, we have presented 55 cases of carcinoma of the gall bladder and 62 cases of carcinoma of the extrahepatic bile ducts. Of our cases of carcinoma of the gall bladder 76.4 per cent were in the female, usually within the sixth or seventh decades; 55 per cent of our cases of carcinoma of the extrahepatic bile ducts were in the male of similar average age.

The clinical syndrome associated with these lesions is not as simple as commonly believed which fact probably explains the frequently incorrect diagnosis. Pain was present in 60 per cent of the cases of gall-bladder carcinoma. Jaundice was present in another 60 per cent of these cases, and gastrointestinal symptoms and cachexia in about 50 per cent. Evidence of edema and ascites was seen in 40 per cent. A palpable liver was found in 63 per cent of these cases whereas a palpable gall bladder was seen in 23 per cent. A profound secondary anemia was the only consistent laboratory finding, being present in 36 per cent of these cases. Of these patients 30 per cent gave a history of previous gall-bladder disease.

Pain of a less severe character was present in 42 per cent of our cases of carcinoma of the extrahepatic bile ducts. Jaundice was seen in 92 per cent and gastrointestinal and cachectic symptoms were elicited in approximately 50 per cent of them. A palpable liver was found in 60 per cent of this group whereas a palpable gall bladder was present in 30 per cent. Approximately 50 per cent of this group gave evidence of edema and ascites. A severe secondary anemia was observed in 30 per cent and chemical blood in the stools in 55 per cent of these patients.

An infiltrating adenocarcinoma is the most frequent type of carcinoma in these neoplasms, a papillary adenocarcinoma being the second most common. Next in order of frequency were the following: scirrhous adenocarcinoma, medullary carcinoma, mucus-producing adenocarcinoma, sarcoma, and one example each of squamous cell carcinoma, round cell carcinoma, and melanoblastoma.

Among the complications of the neoplasm, biliary cirrhosis was by far the most common, followed by cholangitis, empyema of the gall bladder, pericholecystic abscess, liver abscess, hydrops of the gall bladder, biliary peritonitis, spontaneous perforation, and fat necrosis or atrophic fibrosis of the pancreas. Of 55 cases of gall-bladder carcinoma, 36.3 per cent gave evidences of cholecystitis and 72.6 per cent of cholelithiasis. In 3 per cent of the calculous gall bladders a malignancy was present; in 30.6 per cent of the 62 cases of bile duct cancer gallstones were found, and in 22.5 per cent there was evidence of cholecystitis.

In our experience, Courvoisier's law is verified more often by post-mortem examination than by clinical findings; nevertheless, even

autopsy records indicate the inaccuracy of this didactic principle. A distended gall bladder was found in 29 per cent of the necropsies of gall-bladder cancer, and in 62.9 per cent of the necropsies of bile duct cancer.

Evidences of metastases were found at necropsy, varying from involvement of the regional lymph nodes to generalized carcinomatosis, in 96 per cent of our cases of gall-bladder cancer and in 76.7 per cent of bile duct cancers. The liver was the most common site for metastasis. Several examples of hematogenous spread were seen. The tendency for metastasis was not characteristic of any particular histological type of neoplasm.

To date, the surgical treatment of this disease has been unsatisfactory and chiefly limited to palliative procedures.

REFERENCES

1. Boyce, F. F., and McFetridge, E. M. Internat. Surg. Digest. 1936, 21: 67–69.
2. Brule, M. Bull. et mém. Soc. méd. d. hôp de Par., 1926, 1: 1497.
3. Burrows, H. Brit. J. Surg., 1932–1933, 20: 607–629.
4. Cabot. Case 16261. New England J. Med., 1930, 202: 1260.
5. Cooper, W. A. Surg., Gynec. & Obst., 1933, 56: 202.
6. Courvoisier, L. G. Casuistisch-statistische Beitrage zur Pathologie und Chirurgie der Gallenwege. Leipzig: F. C. W. Vogel, 1890.
7. Delbert, P., and Godard, H. Bull. de l'Ass. franç. p. l'étude du cancer, 1928, 17: 347–361.
8. Devic, F., and Gallavardin, L. Rev. de méd., 1901, 21: 557–575.
9. Duval, C. W. J. Exper. Med., 1908, 10: 465–475.
10. Erdmann, J. F. Am. J. Obst., 1919, 80: 618.
11. Idem. Ann. Surg., 1935, 101: 1139.
12. Ewing, J. Neoplastic Disease. 3d. ed. Philadelphia: W. B. Saunders Co., 1928.
13. Fehr, A. Ztschr. f. Krebsforsch. 1930, 32: 367.
14. Fueterrer, G. Chicago M. Rec., 1897, 12: 325.
15. Gioja, E. Bull. d. Soc. med. chir. di Pavia, 1929, 4: 235.
16. Illingworth, C. F. W. Brit. J. Surg., 1935, 23: 4.
17. Jankelson, I. R. New England J. Med., 1937, 217: 85.
18. Judd, E. S., and Baumgartner, C. J. Arch. Int. Med. 1929, 44: 735.
19. Judd, E. S., and Gray, H. K. Surg., Gynec. & Obst., 1932, 55: 308–315.
20. Kazama, Y. Japan. M. World, 1922, 2: 309–312.
21. Lancereaux, M. Semaine méd., 1887, 7: 334.
22. Lazarus-Barlow, W. S. Arch. Middlesex Hosp., 1912, 27: 108.
23. Leitch, A. Brit. M. J., 1924, 2: 451.
24. MacCarty, W. C. Coll. Papers Mayo Clin., 1910, 2: 151–192.
25. Magoun, J. A. H., Jr., and Renshaw, K. Ann. Surg., 1921, 74: 700–720.
26. Marshall, J. M. Surg., Gynec. & Obst., 1932, 54: 6.
27. Mayo, W. J. Med. News, 1902, 81: 1105.
28. Mayo-Robson, A. W., and Dobson, J. F. Diseases of the Gall Bladder and Bile Ducts, Including Gallstones. P. 485. New York: Wood, 1904.
29. McGlinn, J. A. New York Med. J. & Rec., 1911, 93: 519.
30. McLaughlin, C. W., Jr. Canadian M. Ass. J., 1933, 28: 255.
31. Miller, R. H. Boston M. & S. J., 1924, 191: 1074.
32. Mohardt, J. H. Internat. Abstr. Surg., 1939, 69: 440.
33. Moll, H. H. J. Path. & Bacteriol., 1925, 28: 528.
34. Musser, J. H. Boston M. & S. J., 1889, 121: 525.
35. Pallin, G. Beitr. z. klin. Chir., 1921, 121: 84.
36. Poynton, F. J. Brit. M. J., 1917, 1: 483.
37. Ragins, A. B. Am. J. Cancer, 1937, 29: 722–728.
38. Renshaw, K. Ann. Surg., 1922, 76: 205.
39. Rosenthal, S. R. Arch. Surg., 1932, 25: 65.
40. Shapiro, P. F., and Lifvendahl, R. A. Ann. Surg., 1931, 94: 61–79.
41. Shelley, H. J., and Ross, L. I. Arch. Surg., 1932, 25: 65.
42. Smithies, F. Am. J. M. Sc., 1919, 157: 67.
43. Springer, E. Boston. M. & S. J., 1925, 192: 997.
44. Upcutt, H. Ann. Surg., 1912, 56: 710.
45. Vander Veer, E., and Nelms, H. L. Ann. Surg., 1928, 87: 157.
46. Vincent, W. G. Med. Rec., 1917, 92: 933.
47. Wahl, H. R. Med. Clin. N. America, 1924, 7: 1331.

EDITORIALS

SURGERY
Gynecology and Obstetrics

FRANKLIN H. MARTIN
Founder and Managing Editor
1905–1935

LOYAL DAVIS, EDITOR

Associates
SUMNER L. KOCH MICHAEL L. MASON

DONALD C. BALFOUR, *Associate, Editorial Staff*

NOVEMBER, 1941

THE TUMOR CLINIC IN TEACHING HOSPITALS

DURING the past ten years, one of the noteworthy achievements of the American College of Surgeons has been the establishment and organization of the cancer clinic in a large number of the country's general hospitals. At the beginning of this program a minimum standard for cancer clinics was agreed upon and since that time yearly reports have been prepared and published, listing those hospitals which conduct cancer clinics in accordance with the requirements of the College. From a small start this list of approved clinics has steadily increased in size, until, in 1940, it contained the names of nearly 350 hospitals. As a result of the many approved clinics now available throughout the country, and also due to the publicity given them through the various educational programs, vast numbers of cancer patients have benefited enormously. The results of recent cancer research are made available to them, adequate facilities for proper treatment are provided, and the recommendations in each case represent a composite opinion of a group of interested and well trained specialists.

Since many of these cancer clinics have now been in existence long enough for the period of adjustment to have been completed and also for those in charge to have accumulated considerable experience in their management, it is perhaps not amiss to view in retrospect the tumor clinic as it operates in the large general hospitals with medical school affiliations and to appraise this work from the standpoint of the several functions of the hospital and the school.

While the details of organization and conduct of such a clinic may differ in different environments, fundamentally the problems are essentially the same. At the University of Michigan the cancer clinic is under the supervision of a cancer commission or committee created by regential action, and composed of the following specialists, each of whom holds a position of professorial rank in the medical school: pathologist, radiologist, surgeon, internist, gynecologist, urologist, ophthalmologist, otolaryngologist, orthopedic surgeon, dermatologist, neurosurgeon, thoracic surgeon, and an executive officer. Generally speaking the function of this committee is to coordinate and correlate all of the various agencies of the hospital and medical school for the purpose of affording patients afflicted with malignant neoplasms the best possible professional service, whether the problem is one of early and correct diagnosis or exclusively one of treatment. The committee aims to integrate and consolidate the experiences of the entire staff in all matters pertaining to malignant

neoplasms, to evaluate existing forms of therapy, and to consider judicially certain newer methods thought to be worthy of clinical trial.

By means of a close liaison with the social service department and through the assistance of its representatives, provision is made for a thorough and continued follow-up study of cancer patients for the remainder of their lives.

In order to make the data assembled from many sources readily available for study and analysis, a central record system becomes essential. Clinical investigation is thus fostered and in addition to the many special studies constantly in progress, yearly reports of the hospital's cancer experience contain much significant information.

Important among the several activities of the cancer clinic are the clinical sessions or conferences. By means of regularly scheduled tumor conferences, provision is made for centralized, prompt, and efficient consultation service which is available to all of the clinical departments. At the time of the conference all relevant data, for example, x-ray films and microscopic preparations, are available for examination by those in attendance and an expert is present to interpret them. Informal discussion is encouraged and the consultation happily loses much of the austere formality which is unavoidable under the refer system. Each conference is regularly attended by a representative from the departments of surgery, pathology, and radiology. The departments of otolaryngology, ophthalmology, dermatology, medicine, pediatrics, oral surgery, and neurology are represented when patients from these services are presented.

While no attempt is made to usurp the right of any individual department to treat patients regularly assigned to it, as deemed best, nevertheless an attempt is made to bring about a standardized plan of clinical procedure in the matter of handling cancer patients. As the result of these conference gatherings, group opinion on various phases of cancer management begins to crystallize and programs of treatment are developed. At the conferences the joint opinion of the pathologist, the radiologist, and the medical and surgical specialists are expressed in writing for the hospital record before treatment is begun. Information regarding biopsy, various palliative and curative surgical procedures, and the employment of radiation methods becomes widely disseminated throughout the staff. Patients seem to appreciate the thorough individual attention which they receive and, as a rule, are impressed with the judgment and advice handed down by the conference group.

Medical students in small groups attend a certain number of these conferences. By so doing in a limited period of time it is possible for them to witness many more unusual and interesting lesions than would be possible during their regular tour of duty on the wards and in the dispensaries of the various departments. Moreover, they learn from the informal discussions that clinical medicine is not a static affair but that there are differences of opinion among mature and well trained clinicians, and they become aware of the progress which is being made in medicine, as they observe certain changes in policy regarding treatment being put into effect.

Staff members conducting the conferences and attending regularly also are afforded an opportunity to observe a large number of uncommon neoplasms, an experience which provides an excellent background of material with which to elucidate subsequent didactic lectures and systematic presentations. In addition these tumor conferences are important in the field of postgraduate medical education. Referring physicians knowing about the con-

ferences often find it worthwhile to accompany their patients or to attend periodically. As a part in the clinical programs arranged for various visiting medical groups, a "sample" tumor conference has proved to be a popular and instructive exercise. These conferences and the preparations for them, involve a considerable amount of work. Lists of the cases to be presented at each conference must be prepared; periodic reports must be written as to status of patients previously seen by group; social service contact with patients must be made, lesions as they appear at the conference must be photographed, and conference opinions filed in each patient's case record.

The success of the conference depends largely upon the regular attendance, enthusiasm, and energy of those in charge, and upon the co-operation of all members of the staff.

Since there is a certain stigma attached to the term "cancer conference," and since the term "tumor conference" may be objectionable to patients for the same aesthetic reasons, various substitutes have been suggested. "Oncology clinic" is preferred by some. In our own hospital we have agreed upon "Neoplasm Conference," a term which seems to be without opprobrium and which, at the same time, is simple and descriptive.

From this brief review, it becomes quite evident that in its own right, the cancer clinic fulfils well the three important functions of a hospital to which Osler so often referred, namely: the care of the patient, the instruction of the students, and the extension of knowledge.

HENRY K. RANSOM.

COMPOUND FRACTURES AND WOUNDS IN WAR

A CONVERSATION with any of the leaders of surgery in North America today does not have to be a prolonged one to reveal that their minds are much occupied with the practice of their profession under military conditions. Some are engaged in problems of organization, some in problems of surgical research, some in the selection of surgical methods that are to be recommended, and some in the incorporation of all of these phases in manuals of procedure. Civilian surgeons are co-operating to the fullest extent with those in the medical service of the military branches of our Government to assure our soldiers and sailors the best that North American surgery has to offer.

It has been emphasized by Dr. Sumner L. Koch in a recent editorial[1] in SURGERY, GYNECOLOGY AND OBSTETRICS that war surgery differs from peace time surgery only in the conditions under which it is practiced and that not in any way is there a difference in the surgical principles which must be observed. It is true that the exigencies of time and the distances through which wounded men may have to be transported may not permit the immediate application of methods that would constitute first measures under ordinary civil conditions, but this fact in no way invalidates the surgical principles involved.

The Committee of the American College of Surgeons on Fractures and Other Traumas made the treatment of compound fractures and wounds of soft parts its major subject of discussion at its annual meeting in New Orleans, January, 1941. Its discussion culminated in a resolution on these subjects, and the distinguished personnel of that committee commands serious consideration of its conclusions.

The Committee on Fractures and Other Traumas, of the American College of Surgeons, at its executive session in New Orleans, January 11, 1941, adopted the following resolutions in reference to the treatment of compound fractures and wounds in war.

[1]Surg., Gynec. & Obst., 1941, 72: 672–673.

COMPOUND FRACTURES

RESOLVED: That it is the consensus of this Committee that the use of snug-fitting plaster encasements in the initial treatment of acute compound fractures is inadvisable except where the case can be closely and continuously observed.

That early splinting, utilizing fixed traction, should be followed by adequate débridement at the earliest possible time; that such débridement should accomplish removal of all dead and devitalized tissue, eliminating all dead spaces and removing all foreign material.

If chemical sterilization is feasible, the use of aqueous sodium hypochlorite is advised.

That the immediate closure of compound fractures is inadvisable.

WOUNDS

That wounds of soft parts not involving bone, joint, nerve, or tendon, following mechanical and chemical débridement may be closed by secondary suture when the bacteriological check on the wounds proves it permissible.

It is also recommended that the surgical committee of the National Research Council further consider the problem of improving and simplifying practices and procedures after a thorough study of the end-results of cases treated to date and a survey of all available literature.

COMMITTEE ON FRACTURES AND OTHER TRAUMAS

CHARLES L. SCUDDER, Boston, Honorary Chairman
ROBERT H. KENNEDY, New York, Chairman
BOWMAN C. CROWELL, Chicago, Secretary

FREDERIC W. BANCROFT, New York
FREDERIC A. BESLEY, Waukegan
WILLIAM B. CARRELL, Dallas
ISIDORE COHN, New Orleans
H. EARLE CONWELL, Birmingham
WILLIAM R. CUBBINS, Chicago
WILLIAM DARRACH, New York
FRANK D. DICKSON, Kansas City, Mo.
ELDRIDGE L. ELIASON, Philadelphia
WILLIAM L. ESTES, JR., Bethlehem
W. EDWARD GALLIE, Toronto
GEORGE H. GEHRMANN, Wilmington
FRASER B. GURD, Montreal
MELVIN HENDERSON, Rochester, Minn.
OTTO J. HERMANN, Boston
WILLIAM L. KELLER, Washington
NORMAN T. KIRK, Washington
PHILIP H. KREUSCHER, Chicago
WALTER ESTELL LEE, Philadelphia
GEORGE A. LELAND, JR., Boston
PAUL B. MAGNUSON, Chicago
HENRY C. MARBLE, Boston
CLAY RAY MURRAY, New York
JOHN R. NILSSON, Omaha
LLOYD NOLAND, Birmingham
HUBLEY R. OWEN, Philadelphia
JOHN J. PRENDERGAST, Detroit
EDWIN W. RYERSON, Chicago
W. O'NEILL SHERMAN, Pittsburgh
LOYAL A. SHOUDY, Bethlehem
KELLOGG SPEED, Chicago
FREDERICK J. TEES, Montreal
JAMES E. M. THOMSON, Lincoln, Nebr.
CHARLES S. VENABLE, San Antonio
J. HUBER WAGNER, Pittsburgh
JOHN B. WALKER, New York
CASSIUS H. WATSON, New York
ROSCOE C. WEBB, Minneapolis
GEORGE E. WILSON, Toronto
JOHN C. WILSON, Los Angeles
PHILIP D. WILSON, New York

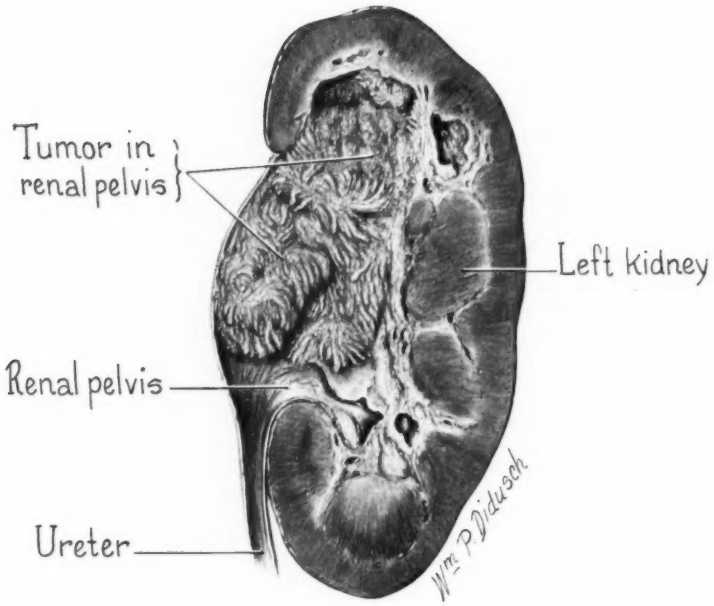


Fig. 1. Papillary carcinoma of the renal pelvis.

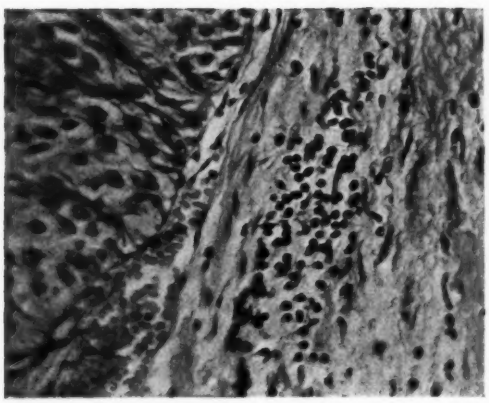


Fig. 6. Section from left renal pelvis, showing typical papillary tumor structure.

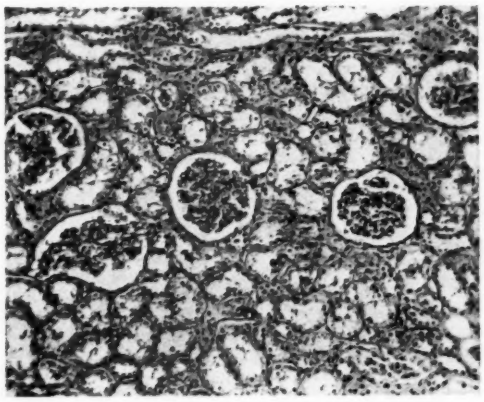


Fig. 7. Section from cortex adjacent to papillary tumor; the tissue is entirely normal.

Papillary Carcinoma of the Renal Pelvis.—Thomas J. Kirwin

UNIV. OF MICH.